Reactance Inversion in persistent asthma: artifact or airway narrowing marker?

Alberto Vidal Grell[1], Ramiro González Vera[2], Jose Castro-Rodriguez[3], and Alejandra Méndez Yarur[1]

[1]Clinica MEDS
[2]Clinica Las Condes
[3]Pontificia Universidad Catolica de Chile Escuela de Medicina

August 12, 2023

Reactance Inversion in persistent asthma: artifact or airway narrowing marker?

Ramiro González Vera MD[1], Alberto Vidal Grell MD[2], Jose A. Castro-Rodríguez MD, PhD[3], Alejandra Méndez Yarur RT[2]

1. Department of Pediatric Pulmonology, Clínica Las Condes, Santiago Chile
2. Department of Pediatric Pulmonology Clínica MEDS, Santiago Chile
3. Department of Pediatric Pulmonology, School of Medicine, Pontificia Universidad Católica de Chile, Santiago, Chile

To the Editor,

Recently Tsukahara et al. published a study of impulse oscillometry (IOS) in a cohort of 22 school-age former preterm children at high risk of bronchopulmonary dysplasia in which reactance inversion (RI) was found in 7 (32%) children. And reported significant differences between inspiratory and expiratory resistance (R) and reactance (X) parameters in children with RI compared to those without RI. They postulated that RI may have a possible pathophysiological cause as tracheobronchomalacia or since it occurs at low oscillatory frequency it may be an artifactual component produced by high respiratory rates (1).

However, R and X are derived exclusively from the impulse test signal. If the technical standards for acceptability and reproducibility are met, ventilatory rate should not influence these parameters. Tsukahara et al. (1) showed only R and X at 10 Hz, but values at 5Hz and other IOS parameters reflecting peripheral airway function like reactance area (AX), resonance frequency (Fres), difference between respiratory R at 5 and 20 Hz (R5-R20), spirometry, and bronchodilator response (BDR) were not included. Therefore, information on lung function in these patients is limited. Notice that the R10 had highest values in the RI group, suggesting more obstructive compromise.

Our group, previously described that RI in children with moderate to severe persistent asthma (n=507, aged 3-18 years) was more frequent in younger children with greater peripheral airway obstruction. In those with RI, the X5 value was highest than expected, the correction X5c, done automatically by Sentry Suite software, correlated better with other IOS parameters reflecting peripheral small airways disfunction (2).

Therefore, to expand these findings, we performed a pilot study on RI in children with persistent moderate and severe asthma. Our hypothesis is that RI occurs mostly in children with narrow or prone to collapse airway as occurs in asthma and especially if they were premature or with low birth weight. The aim of this study was to compare pulmonary function among asthmatic children with and without RI, and between those in whom the RI disappeared versus persisted after the bronchodilator test.

Methods

In the present study we enrolled children with persistent moderate to severe asthma who attended at Clinica Las Condes, Santiago and had pulmonary function tests: oscillometry followed by spirometry performed with a Vyaire Vyntus model v-176430 spirometer-oscillometer and according to ATS/ERS guidelines (3, 4). A systematic medical history on birth weight, gestational age, history of of maternal asthma, and pre and post-natal maternal smoking was obtained. The differences between groups were calculated with the ANOVA test and the post hoc analysis with the Tukey test. The study was approved by the Ethics Committee of the institution; and informed consent was applied to the parents/guardians, and assent to the patients.

Results

We enrolled 57 patients with a mean age of 8.4 years, 59.6% were male. We identified 3 groups of children according with the presence of RI. Group 1 corresponded to 17 (29.8%) patients without RI, group 2 to 17 (29.8%) children in whom RI did not persist after the bronchodilator test, and group 3 to 23 (40.4%) children who had RI before and after the bronchodilator test. The demographic characteristics of the three groups were shown in Table 1. Groups 2 and 3 had lower birth weight and gestational age than group 1; although it was significantly between group 2 vs. 1. No significant differences were found in history of maternal asthma, prenatal or postnatal maternal smoking among groups. Lung function measured by spirometry and IOS was more altered in groups 2 and 3 than in the group 1. VEF1 and FEF25-75 were significantly lower in groups 2 and 3 than in group 1, and FVC was lower in the group 3 vs 1. In the IOS, R5, AX, Fres and DR5-R20 were significantly lower in the group 1 vs. 3. Also, R5 and DR5-R20 were lower in the group 2 vs. 3. In contrast, X5c was significantly higher in the groups 1 and 2 vs. 3, and in the group 2 vs. 3. Finally, RBD in X5c and D5-20 were significant lower in the group 1 vs. 2, and in group 2 vs 3 (Table 2).

Discussion

In this moderate to severe asthmatic schoolchildren, RI was found in a high proportion of the sample (70%). This percentage is similar that we found in a previously published study with high number of participants (2). Results of both studies are concordant and confirm that RI is frequent in schoolchildren with moderate to severe asthma and represents a real peripheral airway condition and not a technical artefact.

Interestingly, there were asthmatic (group 2) in whom RI disappeared after the bronchodilator test, indicating that in these cases it is due to reversible bronchial obstruction; while in others asthmatic (40% of the patients) the RI persisted after the bronchodilator test (group 3). These last group of patients could have a compromised peripheral airway function for different causes, such as increased inflammation, remodeling, or diminished lung function present from birth.

There were also another differences in lung function between these three groups. Patients in group 1 with no prematurity or low birth weight record, had better values in spirometry and in IOS parameters reflecting the peripheral airway function even in X5c. In contrast, lung function was lower in groups 2 and 3. Resistance was increased and the parameters reflecting peripheral airway obstruction were higher in children from groups 2 and 3 than in group 1. Group 3 had highest total airway resistance (R5) and greater small airway compromise (X5c and DR5-R20) than group 2. Besides, group 3 had a lower RBD average in X5c and DR5-R20 than in group 2, which could indicate that group 3 corresponds to asthmatics with a narrow and/or a more collapsible airway associated with prematurity that it persisted until school age.

It has been described that the increase in expiratory resistance and reactance compared to inspiratory may be useful to differentiate asthmatic children from healthy ones or premature children from those born at term and reflects the narrowing of the airways during expiration (5,6). In real life, both conditions may or may not coexist, and in this situation the evaluation of the clinical history, and spirometry becomes important. In the study by Tsukahara et al. (1), the clinical history was not reported, nor spirometry was performed; and an alternative explanation for their finding could be that children with RI were also asthmatic.

Finally, it is important to highlight that in the lung, not only a series resonant structure, but a parallel resonant structure is incorporated. The parallel resonant effect exists in every subject. In children with

obstructive disease, the accessed lung chamber becomes so small that a superimposed parallel resonance is seen. The greater the degree of obstruction, the smaller the pulmonary chamber accessed and the higher the specific parallel resonance frequency. At low frequencies (5 Hz), this will cause the RI phenomenon. In young patients with moderate to severe asthma, obstruction and small peripheral airway may explain why RI occurs. In these cases, the X5 reactance is no longer representative; and the use of "X5 c" would be the most indicated (2). This was also seen in the present study where the basal alterations and bronchodilator response were significant with X5c and not with X5Hz.

Conclusion

RI is a frequent phenomenon exist in moderate to severe persistent asthma children with a history of prematurity or low birth weight, and it is an indicator of alterations in lung function, especially in the parameters that evaluate the function of the peripheral airway. In asthmatics with RI by IOS, it was possible to identify a subgroup with greater peripheral airway obstruction and less bronchodilator response than the group in which the RI disappeared after the bronchodilator test. More studies should be done to confirm these findings.

References

1. Tsukahara K, Scully T, McDonough J, Boas H, DeMauro SB, Ren CL, Allen J. Reactance inversion in a cohort of former preterms: Physiology or artifact? Pediatr Pulmonol. 2023. doi: 10.1002/ppul.26553. Epub ahead of print. PMID: 37341587.
2. Gonzalez Vera R, Vidal Grell A, Yarur AM, Meneses CO, Castro-Rodriguez JA. "Reactance inversion" at low frequencies during lung function measurement by impulse oscillometry in children with persistent asthma. J Asthma. 2022;59(8):1597-1603. doi:10.1080/02770903.2021.1955376
3. King GG, Bates J, Berger KI, Calverley P, de Melo PL, Dellaca RL, Farre R, Hall GL, Ioan I, Irvin CG et al. Technical standards for respiratory oscillometry. Eur Respir J. 2020;55(2):1900753. doi:10.1183/13993003.00753-2019
4. Graham BL, Steenbruggen I, Miller MR, Barjaktarevic IZ, Cooper BG, Hall GL, Hallstrand TS, Kaminsky DA, McCarthy K, McCormack MC et al. Standardization of spirometry 2019 update. An official American Thoracic Society and European Respiratory Society technical statement. Am J Respir Crit Care Med. 2019;200(8):e70-e88. doi:10.1164/rccm.201908-1590ST
5. Sol IS, Kim YH, Kim S, Kim JD, Choi SH, Kim KW, Sohn MH. Assessment of within-breath impulse oscillometry parameters in children with asthma. Pediatr Pulmonol. 2019 ;54(2):117-124. doi: 10.1002/ppul.24201
6. Accorsi BF, Friedrich FO, Corso AL, Rosa JPD, Jones MH. Intra-breath oscillometry for the evaluation of lung function in children and adolescents with a history of preterm birth. J Bras Pneumol. 2022 ;48(1):e20210290. doi: 10.36416/1806-3756/e20210290.

Hosted file

`Table 2 Reactance inversion in persistent asthma artifact or airway narrowing marker.docx` available at https://authorea.com/users/482667/articles/659639-reactance-inversion-in-persistent-asthma-artifact-or-airway-narrowing-marker

Hosted file

`Tables 1 Reactance Inversion in persistent asthma artifact or airway narrowing marker.docx` available at https://authorea.com/users/482667/articles/659639-reactance-inversion-in-persistent-asthma-artifact-or-airway-narrowing-marker