Bronchodilator Response: A Prognostic Indicator for Inhaled Corticosteroid Efficacy in Pediatric Patients with Asthma

Heriberto Martinez MD [1,2], Daniel Lesser MD [1,2,3], Jeremy Landeo-Gutierrez MD, MPH [1,2,3], Kelan Tantisira MD, MPH [1,2,3]

[1]Rady Children's Hospital, San Diego
[2]Department of Pediatrics, University of California San Diego
[3]Division of Respiratory Medicine, Department of Pediatrics, Rady Children's Hospital San Diego

BACKGROUND

- Inhaled corticosteroids (ICS) are the recommended controller therapy of choice for pediatric patients suffering from mild persistent asthma.
- The goal of this study was to identify which asthmatic children were more or less likely to respond to ICS, as defined by improvement in lung function, in the context of a pediatric pulmonology practice.
- We hypothesized that baseline bronchodilator response (BDR) is a significant predictor of an individual's response to ICS.
- Furthermore, individuals with high BDR at baseline will have higher increases in pre-bronchodilator FEV1 percent predicted (FEV1%) between two subsequent office visits while on ICS, compared to individuals with low BDR.

METHODS

- This retrospective study analyzed children with asthma from Rady Children's Hospital San Diego Pulmonary Clinic between 5 and 18 years of age with clinic visits from January 2019 to May 2022.
- Diagnoses of cystic fibrosis, chronic non-asthmatic lung disease, and bronchopulmonary dysplasia were excluded from the study.
- Patients had baseline pulmonary function tests (PFT) with pre and post bronchodilator FEV1% which were used to calculate a BDR before initiating ICS therapy.
- BDR = 100 x (post-bronchodilator FEV1% – pre-bronchodilator FEV1%) / pre-bronchodilator FEV1%.
- High BDR is defined as greater than or equal to 10%.
- Follow-up PFTs obtained at least 3 weeks after initiating ICS were used to asses changes in lung function (change in pre-bronchodilator FEV1%) indicating a response to therapy.

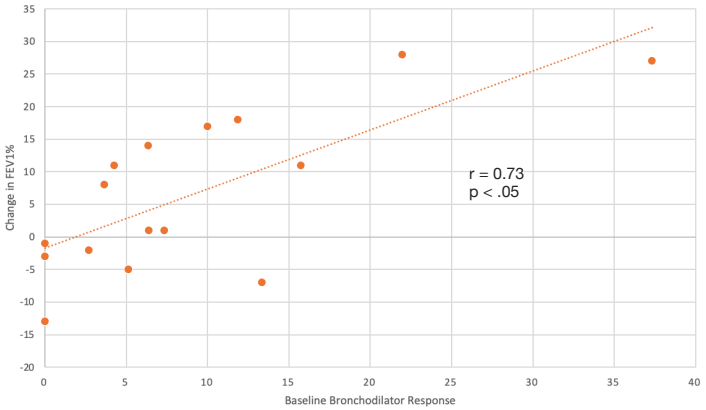
RESULTS

Table 1. Patient Characteristics

Characteristics	Total	High BDR	Low BDR
N (%)	16	6 (37.5)	10 (62.5)
Age (years)	9.5 +/- 3.0**	9.8 +/- 3.7**	9.3 +/- 2.8**
Sex (%)			
Male	10 (62.5)	5 (83.3)	5 (50.0)
Female	6 (37.5)	1 (16.7)	5 (50.0)
Ethnicity (%)			
Non-Hispanic White	6 (37.5)	1 (16.7)	5 (50.0)
Hispanic	9 (56.2)	4 (66.6)	5 (50.0)
Non-Hispanic Asian	1 (6.3)	1 (16.7)	0 (0.0)
Diagnosis (%)			
Reactive Airways Disease	3 (18.7)	2 (33.3)	1 (10.0)
Mild Intermittent Asthma	4 (25.0)	1 (16.7)	3 (30.0)
Mild Persistent Asthma	6 (37.5)	2 (33.3)	4 (40.0)
Moderate Persistent Asthma	3 (18.7)	1 (16.7)	2 (20.0)
Change in FEV1%	6.6 +/- 12.1**	15.7 +/- 12.8**	1.1 +/- 8.0**

**Mean +/- SD

Fig 1. Correlation Between BDR and Change in FEV1%



Baseline BDR and change in FEV1% while on ICS were positively correlated, $r(16) = .73$, $p < .05$.

Table 2. Statistical Analysis

	Total	High BDR	Low BDR	P-Value
Sex (%)				
Male	10 (62.5)	5 (83.3)	5 (50.0)	p = .18
Ethnicity (%)				
Hispanic	9 (56.2)	4 (66.6)	5 (50.0)	p = .26*
Change in FEV1%	6.56 +/- 12.1**	15.7 +/- 12.8**	1.1 +/- 8.0**	p = < .05

*Compared to Non-Hispanic White

**Mean +/- SD

The 6 patients who had high BDR at baseline (M = 15.7, SD = 12.8) compared to the 10 patients who had low BDR (M = 1.1, SD = 8) demonstrated significantly higher changes in FEV1%, $t(16) = 2.8$, $p < .05$, following ICS. Additionally, there was no significant association between sex and BDR, X^2 (1, N = 16) = 1.8, p = .18. Compared to non-Hispanic White patients, Hispanic patients did not differ by BDR, X^2 (1, N = 15) = 1.3, p = .26.

RESULTS

Table 3. Odds Ratio

	Low BDR	High BDR	Total	Odds Ratio
High FEV1% Change*	3	5	8	
Low FEV1% Change	7	1	8	
Total	10	6	16	11.67

*Change in FEV1% greater than or equal to 8% between two subsequent office visits

Patients with high BDR at baseline were 12 times more likely to have a notable lung function response to ICS.

CONCLUSION

- Baseline BDR is associated with response to ICS in pediatric patients with asthma.
- As baseline BDR increases so do the changes between FEV1% in follow up visits while on ICS therapy.
- Patients who have high baseline BDR have significantly higher responses to ICS.
- We have managed to take previous findings from studies done in controlled environments and replicate findings in real-life clinical practice.
- BDR may be an adequate parameter in identifying asthmatic children who could be considered responders to ICS in the real-world clinical setting.

RESOURCES

Bossley, Cara J., et al. "Assessment of Corticosteroid Response in Pediatric Patients with Severe Asthma by Using a Multidomain Approach." Journal of Allergy and Clinical Immunology.

Burke, C. M., et al. "Relative Effects of Inhaled Corticosteroids on Immunopathology and Physiology in Asthma: A Controlled Study." Thorax.

Galant, Stanley P., et al. "The Bronchodilator Response as a Predictor of Inhaled Corticosteroid Responsiveness in Asthmatic Children with Normal Baseline Spirometry." Pediatric Pulmonology.

Landeo Gutierrez, J.S., et al. "Leveraging Electronic Health Records for Evidence-Based Asthma Documentation." B26. Breathe In, Breathe Out: Insights Into Pediatric Asthma.

Ramadan, Amira Ali, et al. "Asthma and Corticosteroid Responses in Childhood and Adult Asthma." Clinics in Chest Medicine.

Sumino, Kaharu, et al. "Variability of Methacholine Bronchoprovocation and the Effect of Inhaled Corticosteroids in Mild Asthma." Annals of Allergy, Asthma & Immunology.

Tantisira, K, et al. "Bronchodilation and Bronchoconstriction: Predictors of Future Lung Function in Childhood Asthma." Journal of Allergy and Clinical Immunology.

Contact:
Heriberto Martinez, MD: h3martinez@health.ucsd.edu
Daniel Lesser, MD: dlesser@rchsd.org
Jeremy Landeo-Gutierrez, MD, MPH: jlandeogutierrez@health.ucsd.edu
Kelan Tantisira MD, MPH: ktantisira@health.ucsd.edu