Original Article

Assessment of Acute Bronchodilator Response in Participants With or Without Airway Obstruction in a Tertiary Care Hospital of West Bengal

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Abstract

Background and Aim: Acute bronchodilator response (BDR) during spirometry is very common in clinical studies. The response varies in different groups of participants. The aim of this study was to analyze the distribution of BDR in participants with or without airway obstruction. **Methods:** A retrospective analytical study of the spirometry results was undertaken. The spirometric values were analyzed for the present study. Among them, 1024 test results were included in our study. The values were estimated by an electronic spirometer, model-RMS Helios-702 in the Department of Physiology, R. G. Kar Medical College, Kolkata on 3200 participants. **Results:** Acute BDR was higher in chronic obstructive pulmonary disease (COPD) participants (45.4%) compared to other participants. Reversibility test was positive in 41.2% of asthma, 31% of allergic rhinitis, 32% of chronic cough, and 13.6% in apparently healthy participants. **Conclusion:** A good percentage of positive BDR is found not only in COPD and asthma but also in allergic rhinitis, chronic cough, apparently healthy participants which indicate its wider utility.

Keywords: Allergic rhinitis, asthma, bronchodilator response, chronic cough, chronic obstructive pulmonary disease, spirometry

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Introduction

The most commonly used pulmonary function test in clinical practice is spirometry. Study of airway responsiveness to a bronchodilator (the reversibility test) during spirometry is also very common in clinical studies. The bronchodilator response (BDR) in reversibility test is a physiological response involving airway epithelium, nerves, mediators, and bronchial smooth muscles.[1] Although much has been learned about BDR, there are some points to be reviewed as for example to enhance its clinical usefulness through proper utilization,[2,3] in the light of its determinants[4] such as participant's cooperation, dose, class, and administration of the bronchodilator and delivery of the drug to the distal airways. Several criteria have been proposed to define a significant BDR.[1,5-10] It is a fact that there is a lack of consensus on the criteria for a significant or increased BDR.[11,12] The most often used criteria for a BDR are those recommended by the American Thoracic Society (ATS), i.e., an increase of 12% or 200 ml in forced expiratory volume in 1 s (FEV_1) or forced vital capacity (FVC) over the baseline value.[6] BDR is used to rule in or rule out asthma and chronic obstructive pulmonary disease (COPD), to predict a patient's response to bronchodilator treatment, to establish best attainable lung function.[13-17] The above cutoff values are used to differentiate asthma and COPD in our institution also.

Generations of students have been taught that asthma and COPD can be differentiated by the BDR test. Evidence over the past few years has raised questions over the application of the reversibility test as a decision-making tool in the areas where it has enjoyed traditional acceptance. Many literatures show

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that reversibility versus irreversibility is not an appropriate approach in making a distinction between the two diseases as irreversible obstruction is also well known in asthma and many COPD patients have a substantial reversibility.[18,19]

The Global Initiative for Chronic Obstructive Lung Disease indicates that, despite earlier hopes, neither bronchodilator nor oral corticosteroid reversibility testing predicts disease progression, deterioration of health status, or exacerbation frequency in patients with a clinical diagnosis of COPD.[20]

Furthermore, the significance of a positive BDR test in normal participants has not been examined. Its significance, when positive in nonobstructive cases also remains to be determined. It is stated that the above cutoff values of reversibility test may not reflect the spectrum of responsiveness in a healthy general population.[11]

On this background, this study was conducted to analyze the reversibility test performed in our laboratory on the participants referred by various departments of our institutions. Therefore, the aim of this study was to analyze the distribution of BDR in the study population with and without airway obstruction.

Materials and Methods

This is a retrospective study conducted at the pulmonary function laboratory, Department of Physiology of R. G. Kar Medical College, Kolkata, after administrative approval.

All the spirometric test results performed between March 2012 and August 2014 on 3200 participants, meeting ATS criteria for acceptability and reproducibility,[6] were considered. Participant's characteristics, including demographics, smoking history, comorbidities, medication used, radiographic findings on chest X-rays, diagnosis and symptoms at the time of the spirometry, were recorded. About 1024 participants with or without significant response to bronchodilators, following inclusion and exclusion criteria as specified below, were included in our analysis. They were grouped into (i) COPD (ii) asthma (iii) allergic rhinitis (iv) chronic cough (v) preoperative and (vi) normal participants.

Inclusion criteria for the cases were (i) clinically stable (ii) diagnosed cases (iii) able to perform technically acceptable spirometry.

Inclusion criteria for the normal participants were (i) apparently healthy participants who came for checkup before Amarnath Jatra without any diseases (ii) normal spirometry.

Exclusion criteria were (i) past or present diagnosis of tuberculosis, chronic bronchitis, lung cancer, restrictive lung diseases, and prior pulmonary resections (ii) clinically unstable patients. (iii) age >90 years and (iv) having less than two acceptable spirometric maneuver.

Spirometry

Pulmonary functions were measured by the electronic spirometer, model-RMS Helios-702 in accordance with the standards of lung function testing of the ATS.[6] The test was explained to the participants and was carried out after a rest for 10 min. The best of the three acceptable results was selected. Postbronchodilator (reversibility test) testing was performed 10 min after administration of the bronchodilator. Spirometric parameters were recorded as a percentage of predicted on reported height and age. Positive response to bronchodilators was defined as a change in FEV_1 or the FVC by at least 12% of baseline.[1]

Statistical analysis

The data were expressed as mean ± standard deviation (SD), and they were analyzed by IBM corp. Released 2011. IBM SPSS (Statistical Package for Social Sciences) Statistics for window, version 20.0. Armonk, NY: IBM Corp. statistical software.

Results

Table 1 shows the baseline characteristics. Mean (±SD) age, height, and weight of the study participants were 42.3 (±17.4), 156.1 (±9.4), and 52.8 (±12.73), respectively. Female participants were more in number (575) than male (449).

Table 2 shows that bronchodilator test was done on (66.99%) of 1024 participants. Reversibility test was advised on 92.3% of allergic rhinitis, 88.6% of COPD, 88.1% of asthma, 80.4% of chronic cough, and 42.9% of preoperative cases. Even 30.9% of the normal participants who came for physical fitness checkup were advised for reversibility test.

Three parameters considered for acute bronchodilator responsiveness on the study groups are shown in Table 3, and 45.4% in COPD, 41.2% in asthma 31% in allergic rhinitis,

Table 1: Baseline characteristics of the study participants

Parameters	*n* (%), mean±SD
Age (years)	42.6±17.4
Height (cm)	156.1±9.4
Weight in (kg)	52.8±12.73
Gender	
Male	449 (43.85)
Female	575 (56.15)

SD: Standard deviation. Data expressed as Mean ±SD

Table 2: Proportion of reversibility test done in different groups

Diseases	Total number of cases	Reversibility test done, *n* (%)	Reversibility test not done, *n* (%)
COPD	149	132 (88.6)	17 (11.4)
Asthma	135	119 (88.1)	16 (11.9)
Allergic rhinitis	130	120 (92.3)	10 (7.7)
Chronic cough	168	135 (80.4)	33 (9.6)
Preoperative	361	155 (42.9)	206 (57.1)
Normal	81	25 (30.9)	56 (69.1)
Total	1024	686 (66.99)	338 (33.01)

COPD: Chronic obstructive pulmonary disease

Table 3: Distribution of positive bronchodilator response in different groups

Diseases	Increase in only FVC	Increase in only FEV_1	Increase in both FVC and FEV_1 (double response)	Positive response, *n* (%)	Negative/no response/ response not significant, *n* (%)
COPD	14	12	34	60 (45.4)	72 (54.6)
Asthma	15	7	27	49 (41.2)	70 (58.8)
Allergic rhinitis	15	2	20	37 (31)	83 (69)
Chronic cough	20	6	17	43 (32)	92 (68)
Preoperative	19	9	30	58 (37.4)	97 (62.6)
Normal	0	2	1	3 (13.6)	22 (86.4)

COPD: Chronic obstructive pulmonary disease, FEV_1: Forced expiratory volume in 1 s, FVC: Forced vital capacity

32% in chronic cough, and 13.6% in healthy showed positive reversibility test.

The proportion of person with acute bronchodilator responsiveness was higher in COPD participants compared to those with reversible airway obstruction and healthy participants. Among persons with COPD, 14 (23.3%) had isolated FEV_1 reversibility, 12 (20%) had isolated FVC reversibility, and 34 (56.7%) had both types. Among persons with asthma, 15 (34.9%) had isolated FEV_1 reversibility, 7 (16.3%) had isolated FVC reversibility, and 27 (62.8%) had both types. Double response (both in FEV_1 and FVC) is more than isolated FEV_1 and FVC reversibility among other diseases also and isolated FEV_1 reversibility is more than isolated FVC reversibility.

Discussion

BDR test during spirometry is typically used to assess the response in cases of obstructive diseases. It is well recognized that the response could be observed in the FEV_1, FVC, or both. BDR was used in clinical trials to rule in or rule out asthma and COPD.[13-17]

There are many factors which affect the reversibility test. Delivery of drug to the distal airways, when given by metered dose inhaler, is an important factor which depends on the size of the particle, inspiratory flow rate, tidal volume, breath holding time, airway diameter,[21] and the technique. It is also reported that more than 50% of the patients using inhalers fail to use proper technique and thus, a small fraction of the drug is inhaled into the lungs.[22] Another important factor is the class and dose of the drug used. One study reported that[22] studied a population sample of 1982 healthy adults using 500 micrograms of terbutaline sulfate and a change of 1.8% from the baseline in FEV_1 was noted. Johannessen *et al*. evaluated FEV_1 and FVC in 515 healthy with 300 micrograms of salbutamol.[23] They have reported an improvement, that is, not constant across age. Older participants have lower reversibility than younger participants. The Lung Health Study (LHS) measured the FEV_1 changes in response to isoproterenol (200 mg) in COPD,[17] they found that 20% of the participants had positive reversibility test.[17] Another study reported over half of a selected COPD population met ATS acute bronchodilator reversibility criteria with salbutamol (400 mg).[24] In the UPLIFT cohort, the majority of patients (53.9%) had positive reversibility test following administration of anticholinergic plus sympathomimetic bronchodilators.[16] In our study, bronchodilator was used as prescribed by the referring physician and in most of the cases it was salbutamol.

In the present study, BDR was observed in various groups of patients referred for spirometry. We did not encounter any evidence of similar systematic BDR test involving so many groups. The results of our study show that the proportion of persons with FEV_1 or FVC acute bronchodilator reversibility was highest in COPD group. This study also showed that positive reversibility test was seen not only in asthma and COPD groups but also in other groups including healthy participants of this study.

Montes de Oca *et al*.[25] showed that of 728 participants with COPD 205 (28%) met the ATS criteria for acute bronchodilator responsiveness, while 523 (72%) were poorly responsive. The LHS measured the FEV_1 changes in response to isoproterenol (200 mg) in mild to moderate COPD.[17] They found that approximately 20% of the participants demonstrated an initial FEV_1 response (200 mL).[17] Other authors reported that over half of a selected COPD population met ATS acute bronchodilator reversibility criteria with salbutamol (400 mg).[24] In the UPLIFT cohort, the majority of patients (53.9%) showed positive reversibility test.[16] In our study, reversibility test was positive in 45.4% of COPD participants, which is consistent with some of these studies[24] but the proportion of patients with positive BDR is higher in our study in comparison with the other studies.[17,22] These differences may be due to the source of the populations studied, type and dose of bronchodilators used.

One study reported[26] that asthmatics showed 78.9% positive BDR as compared to 53.4% positive in COPD. Another study showed that acute BDR was higher in participants of COPD than in asthma.[22] A study by Kuziemski *et al*.[27] showed that reversibility test was positive in 31.9% and negative in 68.1% of patients with asthma. The present study showed that 45.4% of COPD and 41.2% of asthma had positive reversibility test.

In COPD, it has been reported that isolated FVC response is more frequent than FEV_1 response.[16,17] Our findings corroborate with this Chhabra *et al*.,[26] observed a double response and an exclusive FEV_1 response in a greater

proportion of asthmatics whereas in COPD exclusive FVC response was significant.

Allergic rhinitis precedes asthma in many cases, indeed allergic rhinitis may be considered a relevant risk factor for asthma.[28,29] The role of the minimal persistent inflammation in allergic rhinitis might allow the development of structural bronchial remodeling.[30] The present study showed that 31% of allergic rhinitis patients had positive reversibility test whereas Ciprandi *et al*.[31] reported that 62.9% of patients had positive reversibility test. Duration of rhinitis appeared to be a relevant risk factor for the development of impaired lung function[31] and this may be the reason for higher positivity in their study. Anyway, it is clear that the patients with allergic rhinitis should routinely be subjected to reversibility test.

Asthma, postnasal drip syndrome, and gastroesophageal reflux remain the most important causes of chronic cough[32-35] and chronic cough may be associated with one or more of these causes.[34,35] The present study showed that 32% of patients with chronic cough, without asthma have positive reversibility test. Positive BDR test in the present study explains the presence of undetected reversible obstructive elements with chronic cough in these cases. This indicates that the person suffering from chronic cough should be screened by BDR test along with spirometry.

Along with the above, we found reversibility test positive in 37.4% of patients who came for routine pulmonary function test in preoperative checkup. There must be some undetected reversible obstructive elements in these cases also. Hence, there is role of BDR test in these participants.

In the present study, healthy participants who came for checkup before Amarnath Jatra were also advised to BDR test and in them 13.6% showed positive reversibility test with normal spirometry. Khurana *et al*.[22] showed improvement in lung function in about 5% of normal participants. Various explanations have been given for these observations.[36]

Limitations of the study

It should be noted that BDR test has certain limitations also. It is not reproducible. A "nonresponder" on one occasion may be converted to responder on another occasion.[13] The long-term response to bronchodilators cannot be predicted by the acute BDR during the test of reversibility. Even patients with a positive BDR do not differ in mortality, hospitalization, or exacerbation experience from "irreversible" patients.[37] Some studies have indicated that bronchodilator reversibility testing has limited diagnostic value even in differentiating asthma from COPD.[38,39]

Conclusion

BDR test is useful not only for asthma and COPD but also in other cases. Good percentage of positive BDR test in allergic rhinitis, chronic cough, and preoperative cases indicates its wider utility and the cases from these groups should better be subjected to this test. Comparatively, less number of positive cases in most of the groups indicates that there is scope of improving selection of the patient, supervision of administration of the bronchodilator, and optimal effort by the technician to get maximum cooperation from the participants.

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Conflicts of interest

There are no conflicts of interest.

References

1. Pellegrino R, Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R, *et al.* Interpretative strategies for lung function tests. Eur Respir J 2005;26:948-68.
2. Hansen EF, Vestbo J. Bronchodilator reversibility in COPD: The roguish but harmless little brother of airway hyperresponsiveness? Eur Respir J 2005;26:6-7.
3. Vestbo J, Edwards LD, Scanlon PD, Yates JC, Agusti A, Bakke P, *et al.* Changes in forced expiratory volume in 1 second over time in COPD. N Engl J Med 2011;365:1184-92.
4. Lehmann S, Vollset SE, Nygaard HA, Gulsvik A. Factors determining performance of bronchodilator reversibility tests in middle-aged and elderly. Respir Med 2004;98:1071-9.
5. Tashkin DP, Celli B, Senn S, Burkhart D, Kesten S, Menjoge S, *et al.* A 4-year trial of tiotropium in chronic obstructive pulmonary disease. N Engl J Med 2008;359:1543-54.
6. American Thoracic Society. Lung function testing: Selection of reference values and interpretative strategies. Am Rev Respir Dis 1991;144:1202-28.
7. Anthonisen NR, Wright EC. Bronchodilator response in chronic obstructive pulmonary disease. Am Rev Respir Dis 1986;133:814-9.
8. Criteria for the assessment of reversibility in airways obstruction. Report of the Committee on Emphysema American College of Chest Physicians. Chest 1974;65:552-3.
9. Eliasson O, Degraff AC Jr. The use of criteria for reversibility and obstruction to define patient groups for bronchodilator trials. Influence of clinical diagnosis, spirometric, and anthropometric variables. Am Rev Respir Dis 1985;132:858-64.
10. Brand PL, Quanjer PH, Postma DS, Kerstjens HA, Koëter GH, Dekhuijzen PN, *et al.* Interpretation of bronchodilator response in patients with obstructive airways disease. The Dutch Chronic Non-Specific Lung Disease (CNSLD) Study Group. Thorax 1992;47:429-36.
11. Lung function testing: Selection of reference values and interpretative strategies. American Thoracic Society. Am Rev Respir Dis 1991;144:1202-18.
12. Quanjer PH, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R, Yernault JC, *et al*. Lung volumes and forced ventilator flows. Report Working Party Standardization of Lung Function Tests, European Community for Steel and Coal. Official Statement of the European Respiratory Society. Eur Respir J Suppl 1993;16:5-40.
13. Calverley PM, Burge PS, Spencer S, Anderson JA, Jones PW. Bronchodilator reversibility testing in chronic obstructive pulmonary disease. Thorax 2003;58:659-64.
14. Dompeling E, van Schayck CP, Molema J, Akkermans R, Folgering H, van Grunsven PM, *et al.* A comparison of six different ways of expressing the bronchodilating response in asthma and COPD; reproducibility and dependence of prebronchodilator FEV1. Eur Respir J 1992;5:975-81.
15. Nicklaus TM, Burgin WW Jr., Taylor JR. Spirometric tests to diagnose suspected asthma. Am Rev Respir Dis 1969;100:153-9.
16. Tashkin DP, Celli B, Decramer M, Liu D, Burkhart D, Cassino C, *et al*. Bronchodilator responsiveness in patients with COPD. Eur Respir J 2008;31:742e50.
17. Anthonisen NR, Lindgren PG, Tashkin DP, Kanner RE, Scanlon PD, Connett JE; Lung Health Study Research Group. Bronchodilator response in the lung health study over 11 yrs. Eur Respir J 2005;26:45-51.
18. Meslier N, Racineux JL, Six P, Lockhart A. Diagnostic value of reversibility of chronic airway obstruction to separate asthma from

chronic bronchitis: A statistical approach. Eur Respir J 1989;2:497-505.
19. Dow L. Asthma versus chronic obstructive pulmonary disease – Exploring why 'reversibility versus irreversibility' is no longer an appropriate approach. Clin Exp Allergy 1999;29:739-43.
20. Rabe KF, Hurd S, Anzueto A, Barnes PJ, Buist SA, Calverley P, *et al.* Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med 2007;176:532-55.
21. Westfall TC, Westfall DP. Adrenergic agonists and antagonists. In: Brunton LL, editors. The Pharmacological Basis of Therapeutics. 11th ed. United States of America: Goodman and Gilman; 2006. p. 252.
22. Dales RE, Spitzer WO, Tousignant P, Schechter M, Suissa S. *et al*. Clinical interpretation of airway response to a bronchodilator. Epidemiologic considerations. Am Rev Respir Dis 1988;138:317-20.
23. Johannessen A, Lehmann S, Omenaas ER, Eide GE, Bakke PS, Gulsvik A. Post-bronchodilator spirometry reference values in adults and implications for disease management. Am J Respir Crit Care Med 2006;173:1316-25.
24. Ben Saad H, Préfaut C, Tabka Z, Zbidi A, Hayot M. The forgotten message from gold: FVC is a primary clinical outcome measure of bronchodilator reversibility in COPD. Pulm Pharmacol Ther 2008;21:767-73.
25. Montes de Oca M, Perez-Padilla R, Tálamo C, Halbert RJ, Moreno D, Lopez MV, *et al.* Acute bronchodilator responsiveness in subjects with and without airflow obstruction in five Latin American cities: The PLATINO study. Pulm Pharmacol Ther 2010;23:29-35.
26. Chhabra SK, Bhatnagar S. Comparison of bronchodilator responsiveness in asthma and chronic obstructive pulmonary disease. Indian J Chest Dis Allied Sci 2002;44:91-7.
27. Kuziemski K, Jassem E, Slominski JM, Ruczynski J. Assessment of exercise test and bronchial reversibility test as tools for asthma diagnosis in patients with normal spirometry. Przegl Lek 2006;63:1269-72.
28. Guerra S, Sherrill DL, Martinez FD, Barbee RA. Rhinitis as an independent risk factor for adult-onset asthma. J Allergy Clin Immunol 2002;109:419-25.
29. Shaaban R, Zureik M, Soussan D, Neukirch C, Heinrich J, Sunyer J, *et al.* Rhinitis and onset of asthma: A longitudinal population-based study. Lancet 2008;372:1049-57.
30. Ciprandi G, Buscaglia S, Pesce G, Pronzato C, Ricca V, Parmiani S, *et al.* Minimal persistent inflammation is present at mucosal level in patients with asymptomatic rhinitis and mite allergy. J Allergy Clin Immunol 1995;96(6 Pt 1):971-9.
31. Ciprandi G, Signori A, Tosca MA, Cirillo I. Bronchodilation test in patients with allergic rhinitis. Allergy 2011;66:694-8.
32. Poe RH, Harder RV, Israel RH, Kallay MC. Chronic persistent cough. Experience in diagnosis and outcome using an anatomic diagnostic protocol. Chest 1989;95:723-8.
33. O'Connell F, Thomas VE, Pride NB, Fuller RW. Capsaicin cough sensitivity decreases with successful treatment of chronic cough. Am J Respir Crit Care Med 1994;150:374-80.
34. McGarvey LP, Heaney LG, Lawson JT, Johnston BT, Scally CM, Ennis M, *et al.* Evaluation and outcome of patients with chronic non-productive cough using a comprehensive diagnostic protocol. Thorax 1998;53:738-43.
35. Palombini BC, Villanova CA, Araújo E, Gastal OL, Alt DC, Stolz DP, *et al.* A pathogenic triad in chronic cough: Asthma, postnasal drip syndrome, and gastroesophageal reflux disease. Chest 1999;116:279-84.
36. Chhabra SK. FVC response in bronchoreversibility test. Indian J Chest Dis Allied Sci 2001;43:9-11.
37. Albert P, Agusti A, Edwards L, Tal-Singer R, Yates J, Bakke P, *et al.* Bronchodilator responsiveness as a phenotypic characteristic of established chronic obstructive pulmonary disease. Thorax 2012;67:701-8.
38. Chhabra SK. Acute bronchodilator response has limited value in differentiating bronchial asthma from COPD. J Asthma 2005;42:367-72.
39. Kesten S, Rebuck AS. Is the short-term response to inhaled beta-adrenergic agonist sensitive or specific for distinguishing between asthma and COPD? Chest 1994;105:1042-5.