Bronchoconstriction in Response to Deep Inhalation During Spirometry Testing

Jeffrey M Haynes RRT RPFT

Introduction

In healthy individuals, airway resistance has an inverse relationship with lung volume.[1] Moreover, deep inhalation is thought to maintain airway smooth muscle homeostasis and to possess bronchodilating and bronchoprotective properties against challenge agents.[2-6] The bronchodilatory effect of deep inhalation is clearly impaired in asthma patients[2,7,8]; however, the bronchoprotective properties of deep inhalation against challenge test agonists (eg, methacholine) remain robust in many asthma patients with mild airway hyper-responsiveness.[5,6] In some asthma patients, however, deep inhalation can produce paradoxical bronchoconstriction.[5,9,10] This case describes a patient who developed significant bronchoconstriction in response to deep inhalation during spirometry testing.

Case Summary

A 49-y-old white male presented to the pulmonary function laboratory for spirometry, specific airway conductance (sG_{aw}), lung volume testing, and methacholine challenge. The patient had smoked one package of cigarettes/d for 20 y until he quit 1 y before testing. He reported a history of childhood asthma, which had been quiescent throughout his adult life. However, in recent months, the patient reported increasing wheezing and chest tightness after exercise. He noted that symptomatic episodes seemed to occur more frequently following outdoor exercise in cold air. The local temperature on the day of testing was 12°F. According to the patient, a therapeutic trial of albuterol via metered-dose inhaler ameliorated both symptom frequency and severity. An additional asthma risk factor was significant atopy with sensitivities to cats, dogs, horses, pollen, trees, and grass.

On the day of testing, pulmonary function instrumentation passed calibration verifications, and there had been no recent issues with instrument functionality or biologic control testing. The patient demonstrated excellent spirometry technique without evidence of submaximal lung inflation before forced exhalation; however, a progressive decline in the FVC and FEV_1 was observed (Table 1).[11] The patient developed some coughing and reported mild chest tightness. In addition to the progressive decline in numerical values and accompanying symptoms, the emergence of more concave expiratory flow-volume loops further strengthened the suspicion of paradoxical bronchoconstriction in response to the deep inhalation required in spirometry testing. The flow-volume loops from efforts 1 and 6 are superimposed in Figure 1. All spirometry efforts satisfied American Thoracic Society/European Respiratory Society acceptability criteria; however, repeatability criteria were not satisfied as an apparent consequence of progressive bronchoconstriction.[12]

Typically, the largest FVC and FEV_1 should be reported as the best-effort values[12]; however, in this case, it was decided that the largest of the last 3 efforts (effort 6; see Table 1) should be reported as the best effort. The data from all efforts and the technologist's suspicion of deep inhalation-induced bronchoconstriction were shared with the interpreting physician. The rationale for this decision was as follows: Paradoxical bronchoconstriction from deep inhalation was suspected, and the yet-to-be-performed lung volumes and sG_{aw} testing should be linked to data representative of the current state of ventilation. The state of ventilation that accompanied effort 1 no longer existed, and coupling lung volume and sG_{aw} data to a then-nonexistent milieu might be misleading and potentially affect test interpretation. The reported baseline spirometry, lung volume, and sG_{aw} data via whole-body plethysmography are listed in Table 2. Lung volume data indicated signifi-

Mr Haynes is affiliated with the Pulmonary Function Laboratory, St Joseph Hospital, Nashua, New Hampshire.

Mr Haynes has disclosed no conflicts of interest.

Correspondence: Jeffrey M Haynes RRT RPFT, Pulmonary Function Laboratory, St Joseph Hospital, 172 Kinsley Street, Nashua, NH 03060. E-mail: jhaynes@sjhnh.org.

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Table 1. Serial FVC and FEV_1 Measurements During Baseline Spirometry Testing

Effort	FVC (L)	% Predicted*	Z Score*	Change (%)	FEV_1 (L)	% Predicted*	Z Score*	Change (%)
1	5.05	92	−0.61	NA	3.28	76	−1.84	NA
2	4.98	91	−0.71	−1	3.09	72	−2.18	−6
3	4.60	84	−1.23	−9	2.85	66	−2.61	−13
4	4.49	82	−1.38	−11	2.63	61	−3.01	−20
5	4.42	80	−1.47	−12	2.62	61	−3.02	−20
6	4.60	84	−1.23	−9	2.74	64	−2.81	−16
7	4.36	79	−1.56	−14	2.54	60	−3.08	−22

* Based on reference equations by Quanjer et al.[11]
NA = not applicable

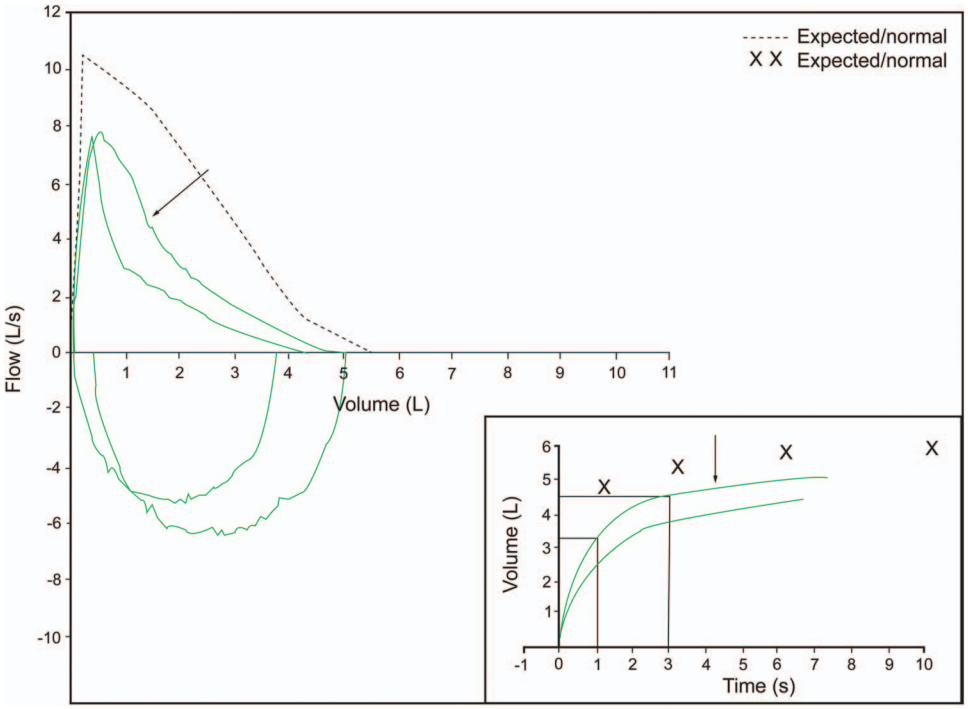

Fig. 1. Superimposed flow-volume loops and volume-time curves from spirometry effort 1 (indicated by arrow) and effort 6. Effort 6 shows lower flows and volumes compared with effort 1.

cant air-trapping with a residual-volume-to-total-lung-capacity ratio of 41%. In addition, the sG_{aw} was below the lower limit of the normal range.

Because of baseline obstruction, the methacholine challenge test was cancelled per laboratory protocol, and bronchodilators (2.5 mg of albuterol and 0.5 mg of ipratropium via small-volume nebulizers) were administered. The patient demonstrated a significant response to bronchodilators with complete reversal of air-trapping and normalization of the FVC, FEV_1, and sG_{aw} (see Table 2). The pre-bronchodilator and post-bronchodilator flow-volume loops are superimposed in Figure 2. It is noteworthy that even if the highest FEV_1 value (3.28 L, effort 1) had been chosen as the best effort, a 24% increase in FEV_1 following bronchodilator administration would have been reported.

Discussion

Spirometric indices are measured to assess lung mechanics and structure via inverse modeling (ie, predict structure from function).[13] Individuals who perform and interpret spirometry tests need to be aware that the deep inhalation required in the test can affect the existing functional state both positively and negatively. Deep inhalation during spirometry testing has the potential to dilate or constrict the airways and protect against bronchial challenge agents (eg, methacholine).[2-10] A lack of appreciation

Table 2. Pulmonary Function Data Pre-Bronchodilator and Post-Bronchodilator

	Pre-Bronchodilator				Post-Bronchodilator			
	Actual	Lower Limit of the Normal Range	% Predicted	Z Score	Actual	% Predicted	Z Score	Change (%)
FVC (L)	4.60	4.3	84	−1.2	5.85	106	0.48	+27
FEV_1 (L)	2.74	3.4	64	−2.8	4.06	94	−0.45	+48
FEV_1/FVC	0.60	0.7	NR	−3.15	0.69	NR	−1.66	+15
TLC (L)	7.81	6.6	101	NR	7.60	99	NR	−3
RV (L)	3.21	3.0*	141	NR	1.72	76	NR	−46
RV/TLC	0.41	0.4*	124	NR	0.23	70	NR	−44
sG_{aw} ([(L/s)/cm H_2O]/L)	0.05	0.1	NR	NR	0.15	NR	NR	+200

* Upper limit of the normal range.
TLC = total lung capacity
RV = residual volume
sG_{aw} = specific airway conductance
NR = not reported

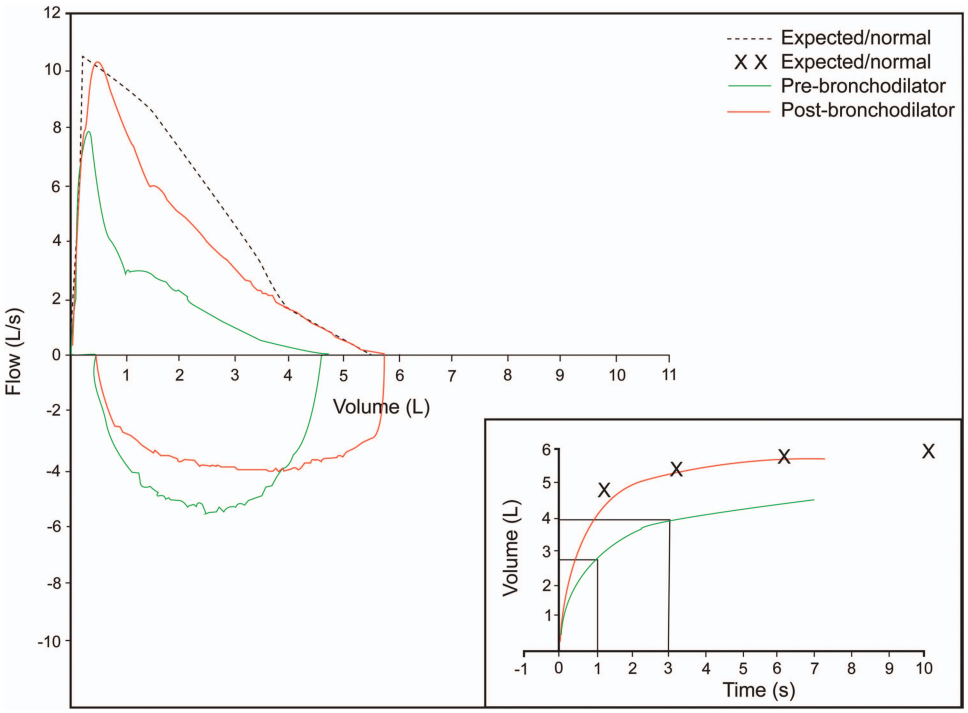

Fig. 2. Pre-bronchodilator and post-bronchodilator flow-volume loops and volume-time curves.

for the potential effects of deep inhalation during spirometry testing may lead to incorrect conclusions regarding the functionality of instruments and the quality of patient test performance. Moreover, the use of a dosimeter methacholine challenge test protocol that encourages inhalation to total lung capacity can result in false-negative challenge tests.[5,6] The obvious danger of any false-negative diagnostic test is misdiagnosis and a misguided treatment plan.

In this case, an asthma patient (as determined by post-test probability) exhibited bronchoconstriction as a consequence of the deep inhalation necessary to perform forced spirometry. Historically, this phenomenon has been attributed to deep inhalation and not the expiratory phase of the maneuver. Moore et al[14] showed no difference in response to methacholine between challenge tests that incorporated repeated exhalation to residual volume (without deep inhalation) and those that prohibited both deep inhalation and forced exhalation. In contrast, Suzuki et al[15] showed a decline in sG_{aw} following an expiratory maneuver from functional residual capacity; however, the decline associated with expiration was smaller than the decline associated with deep inhalation.

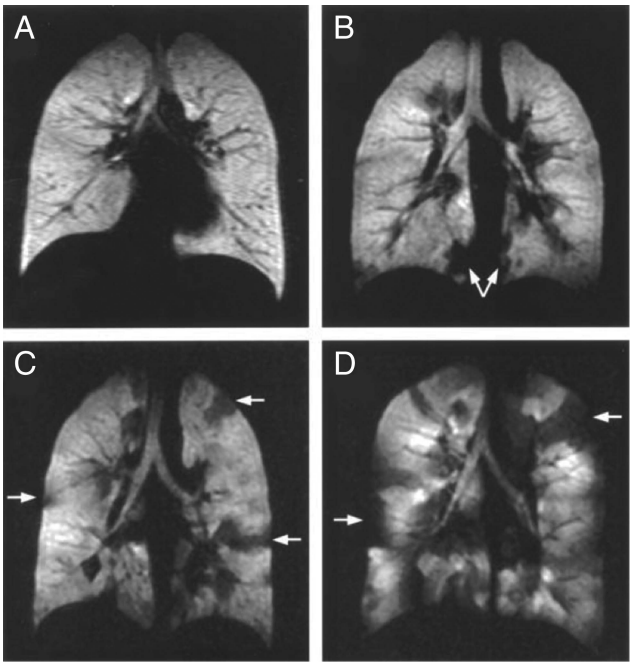

Fig. 3. Magnetic resonance ventilation images after inhalation of hyperpolarized helium. A: Normal volunteer with homogeneous distribution of ventilation. B: Mild asthma. C: Moderate asthma. D: Severe asthma. Arrows indicate ventilation defects. (From Reference 16, with permission.)

The exact mechanism of deep inhalation-induced bronchoconstriction is not completely understood and is presumably multifactorial. Our understanding of the very nature of air-flow obstruction in asthma has been greatly impacted by relatively recent advances in imaging techniques. These imaging techniques have shown that the classic model of relatively diffuse, homogeneous, and predictable patterns of bronchoconstriction are false. In fact, the asthmatic response is one of dynamic heterogeneous bronchoconstriction *and* bronchodilation, which are accompanied by patchy zones of parenchymal hypo-expansion and hyper-expansion, respectively.[16-20] These zones of constricted airways and hypo-expanded parenchyma are referred to as ventilation defects (Fig. 3).[16,20] Through radial traction as a function of airway parenchymal interdependence, the areas neighboring ventilation defects tend to experience bronchodilation and relative parenchymal hyper-expansion. Repeated deep inhalation, especially with limited volume, may be insufficient to expand the ventilation defects, leading to preferential ventilation of the already hyper-expanded zones.[20] This may cause unstable ventilation-defect boundary regions to collapse, resulting in larger and more numerous ventilation defects.

Burns and Gibson[9] theorized that deep inhalation in the presence of obstruction might cause large swings in intrathoracic pressure, resulting in airway edema and worsening airway smooth muscle shortening. To test their theory, they measured sG_{aw} in subjects with asthma and without asthma after deep inhalation with and without a resistive element in situ. Only the subjects with asthma demonstrated significant decreases in sG_{aw} after deep inhalation with added resistance. Lim et al[10] suggested that repeated deep inhalation has the potential to worsen air-flow obstruction as a consequence of reduced deflation recoil. These data should prompt clinicians to exercise caution when asking acutely ill asthma patients to repeatedly perform deep inhalation for spirometry testing, peak-flow measurements, and auscultation.

Teaching Points

- Deep inhalation have the potential to cause bronchoconstriction during spirometry testing.
- Careful observations are necessary to distinguish this phenomenon from instrument malfunction and suboptimal patient effort and technique.
- When bronchoconstriction is observed during spirometry testing, reporting the highest values as the best values may be misleading, especially when these values are linked to tests that are performed after the bronchoconstriction has occurred. The best approach is to show all of the data to the interpreting physician.
- Clinicians should exercise caution when asking acutely ill asthma patients to repeatedly perform deep inhalation for spirometry testing, peak-flow measurements, and auscultation.

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