Pulmonary obstruction in individuals with cervical spinal cord lesions unmasked by bronchodilator administration

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In subjects with spinal cord injury (SCI) a restrictive ventilatory impairment has been well described. Despite numerous studies of pulmonary function in patients with SCI, evidence of an obstructive component of respiratory dysfunction as a result of paralysis has not been observed in this population. We performed spirometry in 34 patients with cervical SCI before and after administration of an inhaled bronchodilator. Significant improvement in flow rate was demonstrated in 14 (41%) subjects. Our results suggest that transection of the cervical spine may result in obstruction to air flow, possibly due to interruption of the sympathetic innervation of the lung with resultant unopposed parasympathetic tone producing bronchoconstriction.

Keywords: quadriplegia; spinal cord injury; pulmonary obstruction; ventilatory impairment; bronchodilator.

Introduction

The degree of respiratory impairment resulting from traumatic injury to the spinal cord is dependent upon the level of injury sustained. Lesions above the third cervical level result in total paralysis of all muscles of respiration, and thereby necessitate mechanical ventilation. Lower lesions will partially spare those inspiratory muscles (diaphragm, scalenes, and sternomastoid) receiving cervical innervation. All muscles of expiration, which are innervated by the thoracic and lumbar spine, are rendered paralyzed by transection of the cervical cord (quadriplegia).

Pulmonary function studies in patients with quadriplegia have documented a restrictive ventilatory impairment, the severity of which parallels the level of injury.¹ Spirometry and measurement of static lung volumes classically reveal significant reductions in vital capacity (VC), inspiratory capacity (IC) and expiratory reserve volume (ERV), as well as elevated residual volume (RV). Measures of air flow, such as the forced expiratory volume in 1 second

(FEV₁) and forced expiratory flow between 25% and 75% of the exhaled volume (FEF_{25–75%}), are also reduced. Because flow rates were always felt to be decreased in proportion to the reduction in VC, the presence of an obstructive component of respiratory dysfunction in this population may not have been suspected by previous investigators.^{2–7}

Transection of the cervical spine interrupts the sympathetic nerve supply to the lungs, which originates from the upper six thoracic ganglia, while parasympathetic innervation, arising from the vagal nuclei of the brainstem with efferent fibers incorporated into the vagus nerve which synapse in ganglia within the airway wall, remains intact.⁸ Such unopposed cholinergic tone accounts for the hypotension and bradycardia associated with cervical spinal cord injury (SCI) and the reported respiratory manifestation of congestion of the sinuses and upper airway,¹ but may also predispose to bronchial smooth muscle constriction and, perhaps, clinically significant airway obstruction.

To further assess the nature of the respiratory dysfunction caused by cervical SCI, we performed pulmonary function studies prior to and after the administration of an inhaled beta-adrenergic agent, metaproterenol, to a group of subjects with quadriplegia.

Methods

Thirty-four male patients with quadriplegia were recruited from the Spinal Cord Injury Service at the Bronx Veterans Administration Medical Center. The study group consisted of 12 nonsmokers (NS), defined as those who had never smoked, and 22 smokers (S), 14 of whom had stopped smoking more than one year prior to the study and 8 of whom were current smokers. The mean age ($\pm$ SEM) of the NS group was 40 ± 5 years and the mean age of the S group was 48 ± 3 years. All 34 patients had complete motor lesions of the cervical spine, 29 (85%) patients had incomplete sensory spinal cord lesions and 5 (15%) had complete sensory lesions. Mean duration of injury ($\pm$ SEM) was 11.8 ± 1.6 years, with

a range of 1–37 years. Upon questioning, 18 (53%) patients reported dyspnea at rest or upon exertion. No subjects displayed evidence of respiratory tract infection or other acute pulmonary symptoms during the course of the study.

Pulmonary function testing was performed with the patients seated upright in their wheelchairs, using a SensorMedics dry rolling seal spirometer. Spirometry was performed before and after inhalation of 2.5 ml metaproterenol sulfate inhalation solution (0.6%). American Thoracic Society (ATS) guidelines for standardization of spirometry were followed.⁹ A significant response to the bronchodilator was defined by criteria established by the ATS as an improvement in $FEV_1 \geq 12\%$.¹⁰ All subjects were able to complete pre- and post-bronchodilator testing.

Results

Results of pre- and post-bronchodilator (BD) spirometry for the study group are subdivided into nonsmokers (NS) and smokers (S) (Table I). Those patients desig-

Table I Pre- and post-bronchodilator (BD) spirometry assessments

PFT		Pre BD	Post BD	% Δ	% Δ Range
<i>Nonsmokers</i> (responders = 5, nonresponders = 7)					
FEV ₁	R	2.30 ± 0.40	2.63 ± 0.43	16 ± 3	(12 to 26)
(l)	NR	2.41 ± 0.23	2.42 ± 0.23	$< 1 \pm 1$	(–5 to 11)
FVC	R	2.71 ± 0.45	2.91 ± 0.41	10 ± 5	(< 1 to 28)
(l)	NR	2.68 ± 0.27	2.69 ± 0.26	$< 1 \pm 2$	(–8 to 11)
FEV ₁ /FVC	R	84 ± 4	89 ± 5		
	NR	91 ± 4	91 ± 4		
FEF _{25–75%}	R	2.89 ± 0.70	3.75 ± 0.82	33 ± 9	(4 to 49)
(l/s)	NR	3.43 ± 0.50	3.73 ± 0.59	11 ± 8	(–21 to 31)
<i>Smokers</i> (responders = 9, nonresponders = 13)					
FEV ₁	R	2.11 ± 0.31	2.33 ± 0.34	16 ± 2	(12 to 30)
(l)	NR	2.50 ± 0.22	2.60 ± 0.23	4 ± 1	(–9 to 11)
FVC	R	2.84 ± 0.35	2.98 ± 0.36	6 ± 2	(–3 to 21)
(l)	NR	3.23 ± 0.23	3.35 ± 0.21	5 ± 2	(–4 to 19)
FEV ₁ /FVC	R	73 ± 3	80 ± 3		
	NR	77 ± 5	77 ± 5		
FEF _{25–75%}	R	1.74 ± 0.37	2.56 ± 0.52	54 ± 10	(10 to 105)
(l/s)	NR	2.69 ± 0.42	2.91 ± 0.52	5 ± 6	(–42 to 33)

Responders (R) are those who had $\geq 12\%$ increase in FEV₁; nonresponders (NR), are those who had $< 12\%$ increase in FEV₁(10). All results are expressed as mean $\pm$ SEM.

nated responders (R) demonstrated a $\geq 12\%$ increase in FEV₁ in response to BD administration.¹⁰ Five of 12 (42%) patients in the NS group, and 9 of 22 (41%) members of the S group demonstrated a significant BD response.

Linear regression analyses between the level of cervical spinal cord lesion (LOL) and the pulmonary function parameters of FVC, FEV₁, and FEF_{25-75%} before and after BD administration were performed. In the NS group, the correlation of FVC and FEV₁ with LOL is positive and significant prior to administration of BD; the correlation becomes more significant post BD (Table II). However, in the S group, FEV₁ and FVC failed to significantly correlate with LOL.

Discussion

Significant improvement of pulmonary function parameters in response to an inhaled bronchodilator strongly suggests the presence of an obstructive component of respiratory dysfunction. In patients with asthma and chronic obstructive pulmonary disease (COPD), airway obstruction is often evident on baseline spirometry, which reveals a decreased FEV₁ to FVC ratio. However, when a restrictive ventilatory impairment is present, as in patients with SCI, the reduced FVC renders interpretation of the FEV₁/FVC ratio difficult, thereby potentially concealing an obstructive defect.

By assessing pulmonary function before and after BD administration, we observed

significant improvement in air flow (FEV₁) in 41% of the smokers and 42% of the nonsmokers. Most of the patients demonstrated a disproportionate improvement in FEV₁ relative to FVC, thereby increasing the FEV₁/FVC post BD. Only in retrospect, after administration of BD, can it be suggested that post-BD spirometry reflects the actual degree of restrictive ventilatory impairment due to SCI, whereas in certain patients pre-BD values may represent the superimposition of restrictive and obstructive impairments. We have previously referred to this phenomenon as 'the unmasking of an obstructive component of respiratory impairment in patients with SCI',¹¹ displayed in the pre- and post-BD spirometry in one of the NS patients (Table III). Pre-BD flow rates and an FEV₁/FVC of 0.80 would be interpreted as quite unremarkable and typical of the restrictive ventilatory impairment resulting from C5-6 lesion. However, after inhalation of BD, FVC remains unchanged while FEV₁ increases by 13%, revealing reversal of underlying airway obstruction. The FEV₁/FVC of 0.90 now reflects the true extent of the restrictive component of this patient and, in retrospect, we are thus able to suggest that the initial FEV₁/FVC of 0.80 is a reflection of the combination of restrictive and obstructive respiratory impairment. Similarly the strong correlation in the nonsmoker group of FEV₁ and FVC with level of lesion improves post BD (Table II), probably as a consequence of elimination of the obstructive impairment, which then allows the SCI-induced restrictive impairment to be measured without other superimposed variables. The variable obstructive component in the smoker group presumably obscures this relationship.

Of particular interest is the significant BD response observed in 5 of 12 (42%) non-smoking patients, who had no history of pulmonary disease or respiratory symptoms prior to their injury. These data suggest that the cervical lesion itself causes some degree of airflow obstruction, most likely secondary to the interruption of sympathetic innervation to the lung and the resultant unopposed parasympathetic tone of the bronchial smooth musculature.

Table II Linear regression analyses between level of lesion and pulmonary function in non-smokers ($n = 12$)

	Pre		Post	
	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>
FVC	0.59	0.04	0.62	0.003
FEV ₁	0.68	0.01	0.72	0.0083
FEF _{25-75%}	0.24	0.46	0.29	0.37

FVC = forced vital capacity; FEV₁ = forced expired volume in 1 second; FEF_{25-75%} = forced expired flow between 25 and 75% of the exhaled volume.

Table III Pre- and post-BD spirometry in a nonsmoking patient

Sample subject: bronchodilator data							
Age	42 years	Diagnosis		C5–6, incomplete quadriplegia			
Sex/Race	Male/Black	Dyspnea		Yes, for 6 yr			
Height	70 in, 178 cm	Cough		No			
Weight	165 lb, 75 kg	Smoking history		Never			
		Pre BD			Post BD		
Spirometry		Pred	Best	% Pred	Best	% Pred	% Δ
FVC	(l)	5.07	3.72	73	3.73	73	< 1
FEV1	(l)	3.84	2.97	77	3.35	87	13
FEV1/FVC	(%)	75	80		90		
FEF _{25–75%}	(l/s)	3.91	2.62	67	3.89	99	48
FEF _{50%}	(l/s)	5.08	2.78	55	4.12	81	48
PEF	(l/s)	9.25	6.65	72	7.58	82	14

FEF_{50%} = forced expiratory flow at 50% of exhaled volume; PEF = peak expiratory flow.

Our results suggest that, in addition to the well documented restrictive ventilatory impairment associated with quadriplegia, an obstructive component of respiratory dysfunction may result from transection of the cervical spine. In cervical SCI patients with respiratory symptoms otherwise unexplained, pre- and post-BD pulmonary function testing may demonstrate the presence of latent airway obstruction. A therapeutic trial of an inhaled beta-adrenergic agent is

warranted in this situation, regardless of the presence of a significant BD response during formal testing, since the sensitivity of the test in this population is not known.

To further investigate the hypothesis that unopposed parasympathetic tone is responsible for cervical SCI-induced airway obstruction, bronchoprovocation challenge testing with an acetylcholine analog should be performed.

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