Exhaled nitric oxide in mustard airway disease

B. Fatemeh Nobakht M.Gh.[1], Rasoul Aliannejad [2*]

1. Department of Basic Medical Sciences, Neyshabur University of Medical Sciences, Neyshabur, Iran
2. Pulmonary Department, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran

Introduction

Mustard airway disease (MAD) is a pulmonary disorder of exposure to sulfur mustard (SM), which demonstrates a broad clinical heterogeneity (1, 2). Several phenotypes of MAD (chronic bronchitis, bronchitis obliterans, asthma, chronic obstructive pulmonary disease (COPD) and so on) were identified amongst subjects who are suffering from late pulmonary complications of SM (2, 3). Since these phenotypes have different therapeutic strategies, differentiating patients may help guiding treatment decision. Therefore, non-invasive approaches are necessary for distinguishing these phenotypes. Fractional exhaled nitric oxide (F_{ENO}) is one of the sensitive, reproducible, and noninvasive inflammatory markers and is elevated in patients with asthma and patients with asthma–COPD overlap syndrome (ACOS) (4, 5). As mentioned above, MAD has a clinical phenotype that shows subjects who manifest features of asthma. However, using F_{ENO} for the identification and management of asthmatic phenotypes of MAD has not been investigated until now.

The aim of this study is to assess the diagnostic performance of F_{ENO}, whether it may be used to discern asthmatic phenotypes of MAD.

Methods

Thirty three patients with MAD were enrolled to assess exhaled nitric oxide (NO) level and its correlation with lung function. From this group, 16 MAD patients with normal symptoms and 17 patients were defined with severe symptoms. Severe patients were receiving inhaled corticosteroids (fluticasone 250–500 mg/salmeterol 25–50 mg per 12 hr) to maintain disease control.

Results

Anthropometric measurements and pulmonary function tests of the study groups were summarized in Table 1.

As shown in Table 1, pulmonary function tests revealed that normal MAD group had significantly higher Forced expiratory volume in 1 second (FEV_1), Forced vital capacity (FVC), and FVC/FEV_1 values compared to severe MAD group. While specific airway resistance (sRA), Functional residual capacity (FRC), Residual volume (RV), and RV/Total lung capacity (TLC) were significantly lower in normal MADs than severe ones.

Our findings showed that exhaled NO levels were higher in sever patients than in normal ones, but not significantly different (Mean Rank: 18 *vs.* 15.94 ppb; $p>0.05$). Furthermore, the results demonstrated that in the severe group, F_{ENO} values have positively correlated with carbon monoxide transfer factor (TLCO). However, we were unable to show a correlation between pulmonary volumes and F_{ENO} levels. We also reported that in severe group 17 percentages of patients had F_{ENO} levels more than 40 ppb (cutoff point of F_{ENO} for asthma patients).

Table 1

	Normal MADs (n=16)	Severe MADs (n=17)	p-value
Age (y)	47.73±1.07	48.52±1.99	p>0.05
Height (cm)	173.0±2.17	171.52±1.73	p>0.05
Weight (kg)	81.6±1.85	74.41±4.85	p>0.05
BMI (kg/m^2)	27.33±0.66	25.25±1.66	p>0.05
FVC (% pred)	80.37±2.93	42.11±4.03	p<0.001
FEV_1 (% pred)	82.12±3.21	32.05±3.3	p<0.001
FVC/FEV_1 (%)	83.31±1.52	63.47±3.54	p<0.001
sRA (% pred)	100.06±16.83	366.0±67.42	p<0.01
FRC (% pred)	102.56±7.25	135.94±11.22	P<0.05
TLC (% pred)	85.0±5.24	86.88±7.02	p>0.05
RV (% pred)	88.75±8.97	185.94±19.03	p<0.001
RV/TLC (%)	100.18±7.8	201.11±9.6	p<0.001
TLCO (% pred)	110.26±7.15	107.66±18.22	p>0.05
KCO (% pred)	130.26±6.16	126.0±11.85	p>0.05
F_{ENO} (ppb)	12.25 (4-29)	19.12 (1-63)	p>0.05

Conclusions

Our findings showed that MAD is a heterogeneous disease based on F_{ENO} results. Exhaled NO could detect asthma phenotype in MAD and it could serve as a useful complement to lung function in the evaluation of MAD. The ranges for F_{ENO} in MAD were mostly similar to COPD. Therefore, we suggested that F_{ENO} levels may help in diagnosis of MAD phenotypes and therapeutic strategies.

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