



Exhaled Nitric Oxide in Chronic Obstructive Pulmonary Disease: Relationship to Pulmonary Function, Disease Severity and Steroid Use.

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ABSTRACT

Fractional exhaled nitric oxide has been used as a pulmonary biomarker in various respiratory diseases, including COPD. There are only a few studies describing the levels of FeNO in COPD patients and some of the published reports are conflicting in their conclusions. Recent studies indicate that FeNO levels correlate with disease severity. There is a relationship between the levels of FeNO in COPD and measures of lung function abnormality. This study is focused on relationship of FeNO levels to lung function, disease severity, differential diagnosis and steroid use.

SUMMARY: There is positive significant correlation between the level of FeNO, Raw and RV/TLC in COPD patients. FeNO measurement is a useful predictive tool for assessing the response to treatment in COPD patients.

KEYWORDS : FeNO, COPD, lung function, severity

INTRODUCTION

There has been interest in the use of non-invasive methods for the assessment of airway inflammation in a variety of lung diseases including chronic obstructive pulmonary disease (COPD).

The role of FeNO in COPD is less clear. FeNO may be raised in COPD (Ansarin et al.2001, Maziak et al,1998, Corradi et al. 1999), although it is lower compared to asthmatic patients. There are only a few studies describing the levels of FeNO in patients with COPD and some of the published reports are conflicting in their conclusions. Also, while some studies reported an increase in the values in patients with stable COPD, others have shown reduced or unchanged values (Ansarin et al.2001, Maziak et al,1998, Corradi et al.1999, Brindicci et al.2005, Clini et al.1998, Rutgers et al.1999, Delen et al.2000, Ziara et al.2003). There is, however, a relationship between the levels of FeNO in COPD and measures of lung function abnormality, as shown by Ansarin et al.2001. Exhaled NO inversely correlated with FEV₁ and was positively correlated with the residual lung volume/total lung capacity ratio in their study (Ansarin et al.2001).

There was a significant positive correlation between FeNO concentrations at admission and the increase in FEV₁ after treatment. There were no correlations between FeNO levels and absolute values for lung function variables at admission or discharge (Balazs et al.2010).

Finally, no study has examined in detail the pulmonary function of COPD patients concurrently, in order to allow assessment of how such variables might influence eNO in either of this disorder. Thus, published studies have described both normal and elevated eNO values in COPD and have suggested both positive and negative correlations between eNO and the severity of airflow limitation. No study has examined the relationship between eNO levels in COPD and ICS use. Exhaled NO levels were higher in COPD patients with partial reversibility of airflow limitation than in those with no reversibility of airflow limitation (Papi et al.2000).

Studies trying to correlate FeNO and the indices of COPD severity have provided conflicting results (Clini et al.1998, Ansarin et al.2001, Bhowmik et al.2005).

Recent studies indicate that levels of FeNO correlate with disease severity (Clini et al.1998).

Brindicci et al., by measuring FeNO at multiple expired flows, have shown that alveolar FeNO is elevated and that it positively correlates with the GOLD Stage.

There was a significant positive correlation between FeNO levels at admission and post-treatment increases in FEV₁ and percent of predicted FEV₁, as well as between FeNO changes during treatment and post-treatment increases in these lung function parameters.

FeNO measurement appears to be a useful predictive tool for assess-

ing the response to treatment in COPD patients with exacerbations (Cowen,2010)

"FeNO measurement is not perfect, but it's useful if you're looking at it in the right context and asking the right question," said D.Robin Taylor, MD, PhD, FRCP, professor of respiratory medicine at the University of Otago in Dunedin, New Zealand (Mullarkey,2010).

PURPOSE OF THE STUDY

To study the practical utility of FeNO values in the diagnosis and management of COPD.

To determine any relationship between FeNO levels in COPD and conventional measures of lung function;

To study the correlation of FeNO values with the degree of obstruction.

To study the correlation of FeNO values with disease severity.

To determine any relationship between FeNO levels in COPD and steroid use.

MATERIAL AND METHODS

This prospective diagnostic study was performed between June 2012 and August 2013 in University Hospital "Shefqet Ndroqi", TIRANA, Albania. In total, 59 subjects with COPD and 67 with Asthma participated in the study. For patients recruited to the COPD group, inclusion criteria were a diagnosis of COPD as defined by the criteria of the American Thoracic Society (ATS) guidelines. Spirometry was performed according to the standards of the ATS. Lung volumes were measured by body plethysmography.

FeNO was measured by an electrochemical nitric oxide analyzer (NIOX MINO); Aerocrine AB, Solna, Sweden). FeNO₅₀ was measured according to the ATS/ERS recommendations (ATS/ERS,2005).

STATISTICAL ANALYSIS

Statistical analyses were performed using SPSS16. Comparisons of mean FeNO values between the groups were performed by ANOVA and unpaired t tests. Paired samples t-test. Pearson's correlation coefficients were calculated to determine the correlation between the FeNO values and continuous data.

RESULTS

The mean of FeNO in Asthma is 53± 50SD. The mean of FeNO in COPD is 10,53± 7,48SD. **The significant difference between them (t-test=6.8, p<0.01)(Fig 1)**

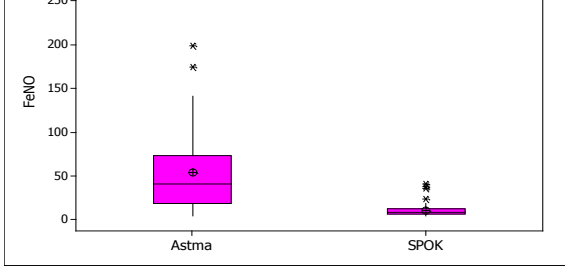


Figure 1. The mean of FeNO in Asthma and COPD.

Among the 59 subjects with COPD the results according to the degrees of obstruction are:

- Normal $8,3 \pm 5,8SD$
- Small airways $13,6 \pm 11,4SD$
- Mild $11,6 \pm 6,1 SD$
- Moderate $10,8 \pm 8,6SD$
- Severe $11,2 \pm 8,6SD$
- Very severe $7,7 \pm 2,1SD$

There is no significant change of the mean of FeNO according to degrees of bronchial obstruction in COPD, ANOVA F-ratio =0.6 p=0.7(- Fig 2)

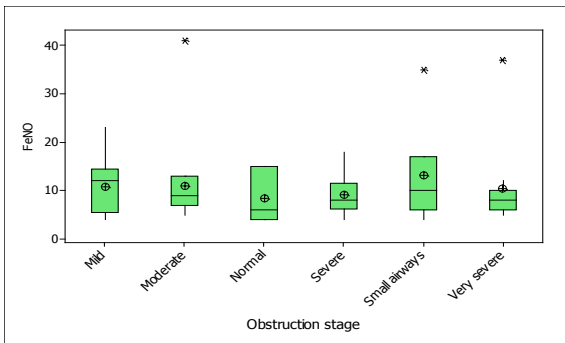


Figure 2. Value of FeNO according of degrees of bronchial obstruction.

The mean of FeNO in COPD was $10,53 \pm 7,48SD$

The mean of FeNO according to GOLD stages in COPD :

- stage A $11,8 \pm 9,4SD$
- stage B $11,0 \pm 8,3SD$
- stage C $7,1 \pm 2,9SD$
- stage D $10,3 \pm 6,5SD$

There is no significant change of the FeNO mean between the stages of COPD. ANOVA F-ratio =0.5 p=0.6(Fig 3)

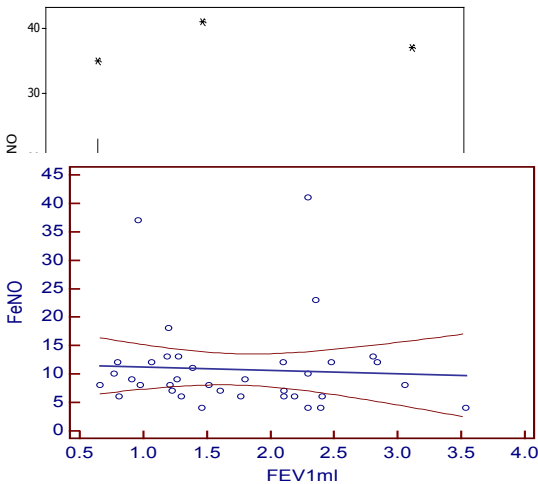


Figure 4. Correlation of FeNO with FEV1

When TLC % increased with one unit, FeNO increase with 0.01 units. ($y= 6.5594 + 0.01562x$) F-ratio=0.4, p=0.5

There is no significant correlation. Fig 5

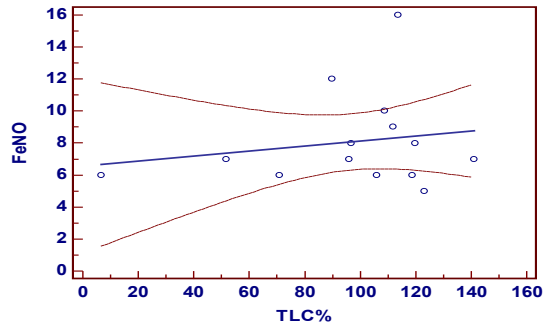


Fig 5. Correlation of FeNO with TLC

When RV % increased with one unit, FeNO decreased with 0.008 unts ($y= 6.8082 + 0.00842x$) F-ratio=0.4, p=0.5

There is no significant correlation (Fig 6)

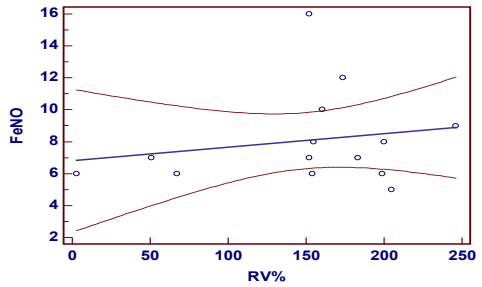


Figure 6. Correlation of FeNO with RV(% dhe ml)

When RV% increased with one unit, FeNO decreased with 0,59 unts ($y=5.8995+0.5960x$) F-ratio=0.5, p=0.5

There is no significant correlation (Fig 7)

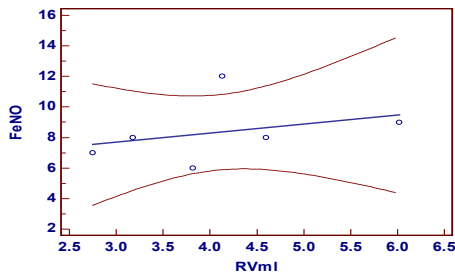


Figure 7. Correlation of FeNO with RV

When RV/TLC increased with one unit, FeNO increase with 0.02 unts, ($y= 6.6178 + 0.02882 x$) F-ratio=0.2, p=0.6 There is positive **significant correlation** (Fig. 8)

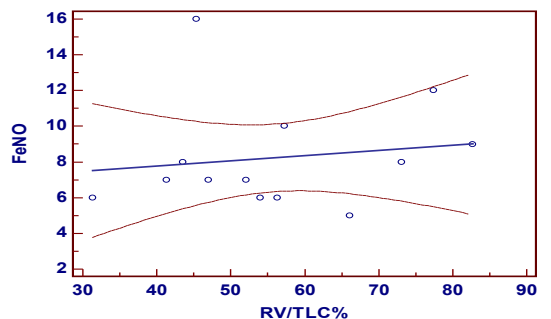


Figure 8. Correlation of FeNO with RV/TLC

When Raw% increased with one unit, FeNO increase with 0.005 unts ($y = 6.0681 + 0.005328 x$) F-ratio=9.9, $p=0.02$

There is positive significant correlation (Fig. 9)

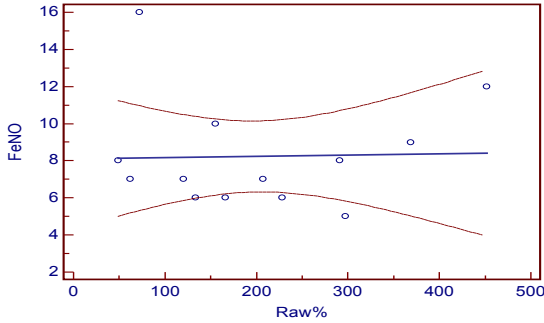


Figure 9. Correlation of FeNO with Raw%

When short term reversibility increased with one unit, FeNO increase with 0.04 unts ($y = 6.0560 + 0.04420 x$) $F = 0.9$ $p=0.3$

There is no significant correlation. (Fig 10)

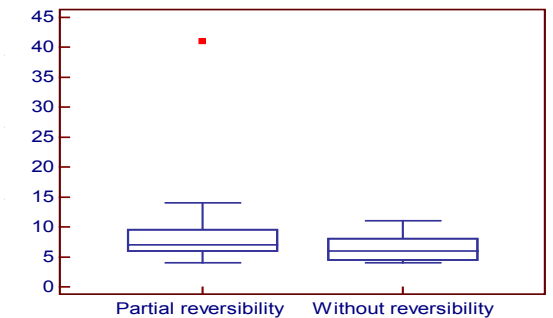
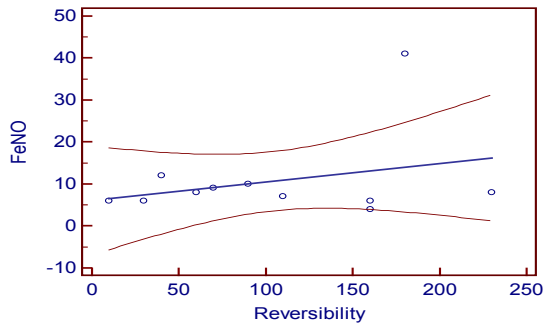


Figure 11. Correlation of FeNO with bronchodilator reversibility to short-acting bronchodilator therapy in COPD

The mean of FeNO before treatment with steroid is $12.3750 \pm 5.9746SD$

The mean of FeNO after treatment with steroid is $6.5000 \pm 2.0000SD$

There is significant difference between them $t = 1.7$ $p = 0.03$

(Paired samples t-test) Fig. 12

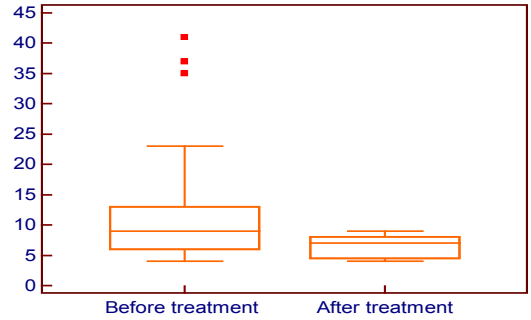


Fig 12. FeNO before and after treatment with steroid in patients with COPD.

DISCUSSION

Recently, attempts are being made to define a biomarker that indicates for acute exacerbation of COPD patients.

That study has shown that in COPD patients with acute exacerbation the mean of FENO is $12.3750 \pm 5.9746 SD$ and after treatment with steroids is $6.5000 \pm 2.0000SD$. There is a significant difference between the mean of FeNO before and after treatment with steroid.

This suggests that patients with COPD show a good response to treatment with steroid during exacerbation.

There is a significant difference between mean values of FeNO in asthma and COPD.

Among patients with COPD, there is no significant change of the mean of FeNO according of degrees of bronchial obstruction and there is also no significant change of the FeNO mean between the stages of COPD.

There is no significant correlation between the level of FeNO and FE-V1, TLC, RV and short term reversibility. The mean of FeNO in patient with partial bronchodilator reversibility is higher

There is positive significant correlation between the level of FeNO, Raw and RV/TLC in COPD patients.

CONCLUSIONS

FeNO is important biomarker in differential diagnosis of asthma with COPD.

There is positive significant correlation between the level of FeNO, Raw and RV/TLC in COPD patients.

FENO may have a role in the monitoring of anti-inflammatory therapy of COPD and can be used to identify patients who may respond to steroids.

FeNO is very useful biomarker in evaluating the efficacy of steroids treatment in exacerbations of COPD patients.

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