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ASTHMA TREATMENT EFFICACY ASSESSMENT BY FeNO MEASUREMENT

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Abstract: *The author of this study tried to demonstrate that exhaled NO measurement is an useful tool in the assessment of asthma: to assess the asthma severity, the presence of symptoms and the assessment of treatment efficacy. The conclusion of the study was the exhaled NO measurement can be significantly correlated with the presence of symptoms, number of symptoms and its intensity and as long as the NO values tend to be as close as possible to the normal values the symptoms are few or no symptom is present and thus, there is an improvement of the quality of life.*

Key words: *asthma severity, exhaled NO, symptoms, quality of life.*

1. Introduction

Asthma is a chronic airway disease characterized by airway obstruction which is caused by a chronic inflammation of the airway and the hyperresponsiveness of this inflamed airway. As a result of this inflammation via interleukin-4/interleukin 12 pathways there is a stimulation of iNOS (inducible nitric oxide synthase) production in the airway epithelium which can cause an increase of NO (nitric oxide), especially among those with atopic asthma.

NOS is present in the paranasal sinus and nasal sinus epithelium and produces nasal NO. Thus, NO comes from two sources, the nasal and paranasal epithelim and respiratory airway epithelium [4, 5]. For the assessment of the inflammation of the respiratory airway it is used the NO produced by the airway epithelium and thus is measured by the fraction of the exhaled NO (FeNO) through mouth. The air exhaled contains NO in small quantities so the measurement unit proposed to quantify this quantity is parts per billion (ppb) [7, 8]. The measurement of NO can be done using one of the following methods: chemiluminescence, electroche-mical sensing and laser spectroscopy [11]. A value of FeNO $\geq$ 25 ppb is considered to be the highest level of NO from which onward an inflammation of the respiratory airway is defined as present. There are two types of factors which may influence the measurement of exhaled NO: technical and breathe maneuver related factors and patient related factors. Among technical and breathe maneuver related factors are inspiration manoeuvre, breath hold, exhalation flow rate, exhalation time, oral pressure and ambient NO. Among patient related factors the most important are allergic sensitization, smoking history, spirometric manoeuvres. Thus, it is very important that these factors should be avoided as much as possible or minimalized to as low as possible to have a smaller impact over the measurement of NO [1], [6].

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2. Objectives

The objectives of this study that have been pursued are clinical evolution assessment of asthma, the degree of association between FeNo and patient's symptoms and the assessment of treatment efficacy through serial measurements of FeNO among successive visits.

3. Material and method

This study has been performed at Pneumology Hospital from Brasov during November 2008 and September 2010. It has been selected a number of 40 patients of different ages (15 – 82 years old) and gender who have been individualy monitored for 3 months.

Clinical assessement has been done using asthma questionnaires, spirometry and NO measurement.

Inclusion criteria are:

- a diagnosis of asthma recently discovered;
- patients able to perform acceptable spirometry and FeNO measurement;
- initial FeNo value equal to or more than 25 ppb;
- patients compliant to treatment and visit schedule.

NO measurement has been performed initial to check the inclusion criterion and it has been repeated after one month, two months and three months (this is the final evaluation) from the initial assessment during this time patient kept taking their asthma medication (maintenance medication as well as the rescue medication) which has been initiated at the initial visit. At each clinic visit, patient filled in the asthma questionnaires to assess the evolution of symptoms.

FeNO measurements have been performed using a portable NIOX MINO device which uses the electrochemical, method to determine the NO.

Used degrees of asthma are: intermittent, mild persistent, moderate persistent and severe asthma.

Inflammation classification by the NO is as it follows: mild inflammation between 25 and 39 ppb, intermediate inflammation between 40 and 59 and severe inflammation above 60 ppb [1, 2, 3].

4. Results and discussion

At the initial assessement all 40 patients have had symptoms. The most frequent symptoms are: cough, wheezing, dyspnoea, nasal congestion, nasal itch, rhinorrhea, sneeze and watery eyes. These symptoms are suggestive for the association between asthma and allergic rhinitis, the last condition being frequently met in correlation with asthma.

42.5% of the patients have had present 6 to 8 symptoms in various associations, 40% of the patients have had 3 to 5 symptoms and only 17.5% of the patients have had 1 to 2 symptoms.

The portable NIOX MINO device is able to measure the FeNO at a range of 5 to 300 ppb.

Initial measurement of NO revealed that 35% of the patients have had mild airway inflammation, 17.5% moderate airway inflammation and 42.5 have had a severe airway inflammation. Among patients with intermittent asthma the average FeNo was 37.3 ppb while among mild asthma and intermediate asthma the average FeNO was 50.6 ppb, respectively 64.7 ppb. There was only one case, a particular one which has had a FeNO value of 300 ppb which the maximum value measured by the portable NIOX MINO device. This case has had also the most symptoms and worst ones thus having a very high degree of airway inflammation. Among those patients with severe asthma the FeNO average was 96.7 ppb. Patients with intermittent asthma have lower average FeNO values towards the other degrees of asthma severity and patients with severe persistent asthma have higher average FeNO values which are different from those recorded by moderate asthma and mild persistent asthma.

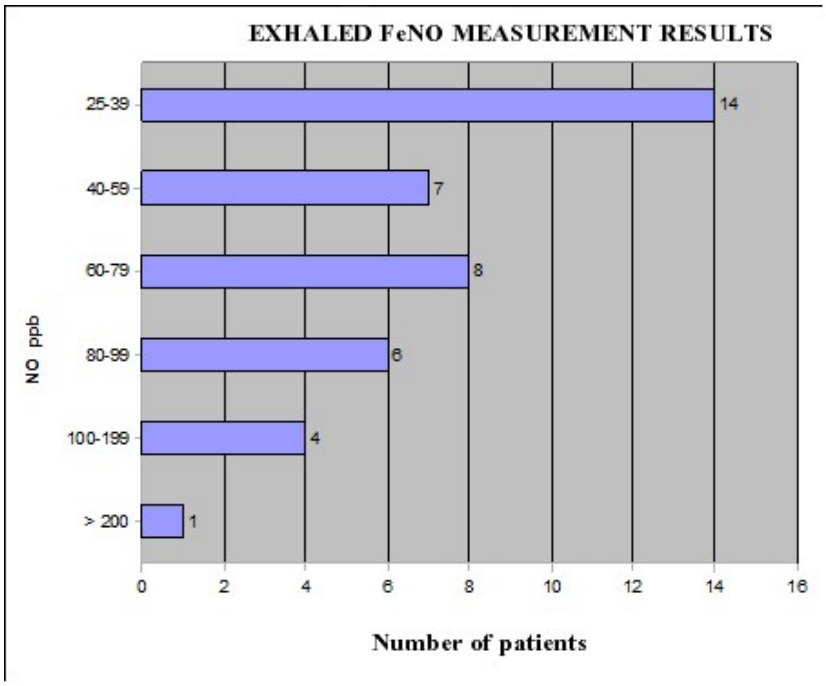

Fig. 1. *Initial results of FeNO measurement*

At the and of our study 35% of the patients have had no symptoms and the number of symptoms has considerably decreased to half among 65% of them and no patient experienced more than 4 symptoms compared to the start of the study when all the patients have has symptoms.

Analyzing the correlation between symptoms and the visits we observed that the average symptoms decreased from 4.72 to 1.84. During the initial visit the average number of symptoms was 5, at the second visit decreased to 3-4 symptoms and at the third visit the number was 2-3 symptoms.

At the end of the 3 months study the patients have had an improvement of the quality of life, thus having none or 1-2 symptoms. During the 3 month evaluation, patients have had a favourable evolution with a decrease trend in severity and a change of the degree of severity. Thus has been recorded a migration of the patients from severe asthma to intermittent asthma and during the first period of evaluation the average was moderate persistent asthma and at the end of the study the average was intermittent asthma having a significantly statistically calculus ($p<0.001$ and $r=0,705$).

Final results of exhaled NO measurements Table 1

NO interval	Number of patients	Percentage
25-39	33	82,5%
40-59	6	15%
60-79	0	0%
80-99	0	0%
100-199	1	2,5%
>200	0	0%

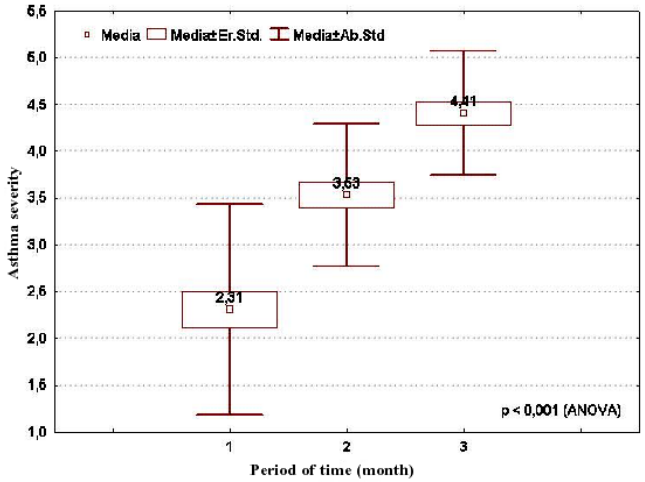

Fig. 2. *Asthma severity evolution among three months of monitoring*.

At the final FeNO measurement we have observed a smaller value of the exhaled NO and consecutively the airway inflammation has registered a decrease. Values have normalized in 65% of the patients with a range of 5 to 24 ppb. Only 14 patients which represent 35% of all patients still have an increased value of FeNO (25 – 57 ppb). Of those 65% with normal values of exhaled NO more than half of them (53.8%) have no symptoms at the end of the study as shown above.

The particular case with an initial exhaled NO value of 300 ppb has had at the final evaluation visit an exhaled NO of 147 ppb with less symptoms, less intense symptoms and a significantly general improvement. The calculus it is significantly statistically $p< 0.001$.

We calculated also the average value of exhaled NO among visits and the results are significantly statistically between visit 1 and 3 and visit 2 and 4 ($p<0,001$). The average exhaled NO value is as it follows: at visit 1 (initial) is 70, at visit 2 is 51.6 ppb, at visit 3 is 43.3 ppb and at the end it is 28.5 ppb.

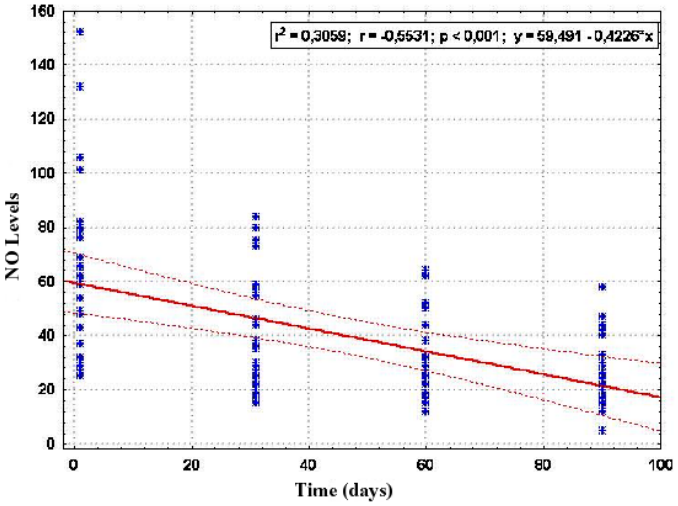

Fig. 3. *NO levels regression curve*

The maintenance treatment of the studied patients was represented by inhaled corticosteroids, combinations of long acting beta agonists and inhaled corticosteroids and leukotriene receptor antagonist and as rescue medication it has been used short acting beta agonists.

In our study, there was a decrease of average intensity of symptoms and also there was a reduction among the number of present symptoms comparing the start of the study with the end of the study. Similar results were obtained by Marcello Verini et al., in their study performed on 32 children in Chiety, Italy which has had duration of one year and they used FeNO to assess its usefulness in the evaluation of asthma treatment. They also reached the conclusion that there is a reduction of symptoms experienced by patient but also the exacerbations. In our study we demonstrated a decrease of the symptoms and number of symptoms among children as well as adults. Marcello Verini et al. have also reached the conclusion that FeNO measurement can be used to assess the efficacy of asthma treatment can help the guidance of treatment in asthma management [1], [10]. In our study, we have proven that the FeNO can be used to assess the treatment efficacy in adults as well as among children. M.W. Pijnenburg et al. have also indirectly demonstrated that FeNO can be used as a noninvasive method to assess the treatment efficacy by performing a study in which they stopped the treatment and measured the FeNO and assessed the symptoms because there was an increase in FeNO value and a relapse of asthma symptoms [1], [9].

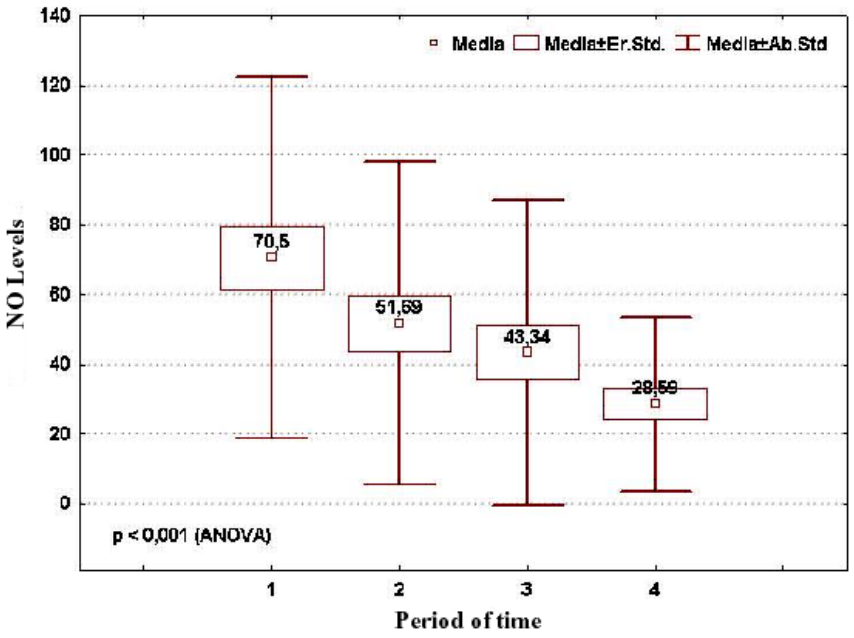

Fig. 4. *NO average value evolution along 3 months of monitoring*

5. Conclusion

1. Maintenance medication monitoring is able to better classify the severity of asthma and NO measurement is able to provide the necessary information.

2. There is a significant degree of association between symptoms improvement and the continuous decrease of exhaled NO values, thus, making NO measurement an useful tool regarding the asthma symptoms evolution and treatment efficacy assessment.
3. Exhaled NO measurement through NIOX MINO device is a simple, valid, noninvasive and quick method to evaluate asthma severity and asthma control.
4. Exhaled NO measurements to assess the asthma treatment efficacy and asthma control can be used in both children and adults.
5. The lower the value of exhaled NO value is the fewest symptoms are present and thus, there is an improvement of quality of life.

References

1. Luca, A.: *Monitorizarea tratamentului şi a evoluţiei astmului bronşic*. Lucrare de diplomă. 2012.
2. Shaw, D.E., Wilson, E., Pavord, I.D.: *Exhaled nitric oxide in asthma.* In: Exhaled Biomarkers. In: Eur Respir Mon 2010. 49, 32–44.
3. Turktas, H., Oguzulgen, K., Kokturk, N., et al.: *Correlation of exhaled nitric oxide levels and airway inflammation markers in stable asthmatic patients*. In: J Asthma. 2003; 40: 425–430.
4. Lundberg, J.O., Rinder, J., Weitzberg, E., et al.: *Nasally exhaled nitric oxide in humans originates mainly in the paranasal sinuses.* In: *Acta Physiol Scand* 1994; 152: 431–432.
5. Lundberg, J.O., Farkas-Szallasi, T., Weitzberg, E., et al.: *High nitric oxide production in human paranasal sinuses.* In: *Nat Med* 1995; 1: 370–373.
6. Alving, K., Malinovschi, A.: *Basic aspects of exhaled nitric oxide.* In: *Exhaled Biomarkers*. In: Eur Respir Mon. 2010. 49, 1–31.
7. Alving, K., Weitzberg, E., Lundberg. J.M.: Increased *amount of nitric oxide in exhaled air of asthmatics*. In: *Eur Respir J* 1993; 6: 1368–1370.
8. Gustafsson, L.E., Leone, A.M., Persson, M.G., et al.: *Endogenous nitric oxide is present in the exhaled air of rabbits, guinea pigs and humans*. In: *Biochem Biophys Res Commun.* 1991; 181: 852–857.
9. Pijnenburg, M. W., Hofhuis, W., Hop, W. C., De Jongste, J. C.: *Exhaled nitric oxide predicts asthma relapse in children with clinical asthma remission.* In: Thorax 2005; 60:215–218. doi: 10.1136/thx.2004.023374.
10. Verini, M., et al.: *FeNO as a Marker of Airways Inflammation: The Possible Implications in Childhood Asthma Management.* In: Journal of Allergy Vol. 2010, doi:10.1155/2010/691425.
11. Silkoff, P.: *History, technical and regulatory aspects of exhaled nitric oxide*. In: J Breath Res 2008; 2: 037001.