Significance of fractional exhaled nitric oxide in chronic eosinophilic pneumonia: a retrospective cohort study

Ji Young Park1,2, Taehoon Lee1,2, Hongyeul Lee1,2, Yeon Joo Lee1,2, Jong Sun Park1,2, Young-Jae Cho1,2, Ho Il Yoon1,2, Jae Ho Lee1,2 and Choon-Taek Lee1,2*

Abstract

Background: Chronic eosinophilic pneumonia (CEP) is characterized by chronic eosinophilic infiltration of the lung. It is dramatically responsive to corticosteroid treatment, but symptoms and radiopacities recur frequently after tapering or discontinuing the medication. Fractional exhaled nitric oxide (FeNO) is a well-known noninvasive marker of eosinophilic airway inflammation. The aim of this retrospective cohort study was to investigate the relationships of FeNO with peripheral eosinophilia and the clinical state of CEP and its validity for predicting exacerbation of CEP.

Methods: Standard clinical and laboratory parameters, peripheral eosinophil percentage and count, and FeNO level were measured in 18 patients with CEP at several assessment points over 1 year.

Results: FeNO level was positively correlated with peripheral eosinophil count (r = 0.341, P = 0.005) and percentage (r = 0.362, P = 0.003). The median (IQR) FeNO levels were 79 (41–88) and 35 (26–49) ppb in uncontrolled (13/74 measurements) and controlled (61/74 measurements) CEP, respectively (P = 0.010). The FeNO level of 66.0 ppb showed the largest area under the curve (0.835) for predicting exacerbation of CEP (sensitivity = 0.80, specificity = 0.84).

Conclusion: FeNO may be useful for monitoring eosinophilic parenchymal inflammation and determining the appropriate corticosteroid dose in CEP.

Keywords: Chronic eosinophilic pneumonia, Fractional exhaled nitric oxide, Biomarker, Corticosteroid

Background

Chronic eosinophilic pneumonia (CEP) is a rare disease of unknown cause. It is characterized by chronic respiratory symptoms, bilateral peripheral lung opacities, pulmonary eosinophilia, and/or peripheral eosinophilia. CEP shows a dramatic response to corticosteroids. Symptoms and radiopacities resolve rapidly after corticosteroid treatment [1], but they recur frequently after tapering or discontinuing the medication [1,2]. Most patients need prolonged tailored treatment, similar to those with asthma [3]. Therefore, a marker is required to assist in monitoring and controlling CEP.

FeNO is an important marker of eosinophilic airway inflammation in diseases such as asthma and nonasthmatic eosinophilic bronchitis [4]. In asthma, FeNO level is significantly correlated with eosinophil counts in bronchoalveolar lavage (BAL) fluid, induced sputum, and airway mucosal tissue [5-7]. It can identify patients with asthma who are likely to benefit from corticosteroid treatment and have reduced exacerbation rates [8-10]. Transition of asthma from the well-controlled to the poorly controlled state is associated with a rise in FeNO level [11]. Further, maintenance doses of inhaled corticosteroids can be reduced without loss of asthma control on the basis of FeNO level [12,13]. However, its value in eosinophilic parenchymal lung disease is unknown because inducible
nitric oxide synthetase, the major source of FeNO, is usually found in airway epithelium [14]. Recently, our group reported that FeNO level is significantly higher in patients with acute eosinophilic pneumonia (AEP) than in those without AEP and decreases during corticosteroid treatment, strongly suggesting that FeNO level increases in eosinophilic parenchymal lung diseases [15]. Further, FeNO level is lower in patients with stable bronchiectasis than in those with asthma or chronic obstructive lung disease, implying that FeNO has no role in neutrophilic airway inflammation [16]. In this study, we explored the significance of FeNO in the diagnosis and management of CEP, an eosinophilic lung parenchymal disease, by investigating its relationships with peripheral eosinophilia and the clinical state of CEP and its validity for predicting exacerbation of CEP.

**Methods**

**Study design and definitions**

This retrospective cohort study was conducted at Seoul National University Bundang Hospital between November 2011 and October 2012. The Institutional Review Board approved the study protocol and waived the need for informed consent from patients (B-1210-174-105).

Diagnosis of CEP was based on the following criteria: (i) pulmonary opacities with peripheral predominance on chest radiography; (ii) peripheral eosinophilia ≥ 1000 cells/μL and/or alveolar eosinophilia ≥ 40% of the eosinophil count in BAL fluid; (iii) respiratory symptoms for over 2 weeks; and (iv) exclusion of known causes of eosinophilic pneumonia (parasitic infection, drugs, or allergic bronchopulmonary aspergillosis), eosinophilic granulomatosis with polyangiitis (Churg–Strauss syndrome), and hypereosinophilic syndrome [1].

Exacerbation was defined as reappearance of characteristic infiltrates on chest radiography, recurrence of typical clinical features, and increasing peripheral eosinophilia. Uncontrolled CEP was defined as administration or increasing dosage of corticosteroids due to diagnosis or exacerbation of CEP. Controlled CEP was defined as absence of symptoms regardless of corticosteroid dose.

**Measurements**

At each visit during the 1-year study period, we assessed symptoms, chest radiographic findings, peripheral eosinophil count and percentage, and FeNO level. The recall interval was individualized according to the clinical state: most patients were reexamined every 2–3 months, but some patients with uncontrolled CEP were recalled before the scheduled appointment. Change in FeNO levels between visits was calculated at every assessment point, as follows: \( \Delta \text{FeNO} = \text{FeNO}_n - \text{FeNO}_{n-1} \), where \( n \) and \( n - 1 \) represent the \( n \)-th and preceding visits, respectively. Changes in peripheral eosinophil count (\( \Delta \)eosinophil count) and percentage (\( \Delta \)eosinophil percentage) were similarly calculated.

FeNO level was measured by using a NIOX MINO monitor (Aerocrine AB, Solna, Sweden), without the nose clip, at an exhalation flow rate of 50 mL/s, according to the American Thoracic Society (ATS)/European Respiratory Society (ERS) recommendation [17].

| Variable                                                                 | Value*                         | Number reported/tested |
|--------------------------------------------------------------------------|--------------------------------|------------------------|
| Age (years)                                                              | 56 (41–68)                     | 18                     |
| Disease duration (months)                                                | 19.1 (9.9–28.7)                | 18                     |
| Gender                                                                   |                                |                        |
| Female                                                                   | 8 (44.4)                       | 8 (44.4)               |
| Male                                                                     | 10 (55.6)                      | 10 (55.6)              |
| Smoking status                                                           |                                |                        |
| Current smoker                                                           | 1 (5.6)                        | 1 (5.6)                |
| Ex-smoker                                                                | 4 (22.2)                       | 4 (22.2)               |
| Pack-year history                                                        | 25 (20–40)                     | 25 (20–40)             |
| Symptoms or signs                                                        |                                |                        |
| Cough                                                                    | 15 (83.3)                      | 15 (83.3)              |
| Sputum                                                                   | 13 (72.2)                      | 13 (72.2)              |
| Dyspnea                                                                  | 5 (27.8)                       | 5 (27.8)               |
| Fever                                                                    | 2 (11.1)                       | 2 (11.1)               |
| Wheezing                                                                 | 4 (22.2)                       | 4 (22.2)               |
| Crackle                                                                  | 3 (16.7)                       | 3 (16.7)               |
| History of tuberculosis                                                  | 1 (5.6)                        | 1 (5.6)                |
| Laboratory findings                                                      |                                |                        |
| White blood count (cells/μL)                                            | 8060 (7470–9660)               | 18                     |
| Peripheral eosinophil percentage (%)                                     | 21.2 (11.6–42.3)               | 18                     |
| Peripheral eosinophil count (cells/μL)                                   | 1543 (771–4034)                | 18                     |
| Eosinophil percentage in BAL fluid (%)                                   | 47 (15–65)                     | 7                      |
| C-reactive protein (mg/dL)                                               | 1.5 (0.30–3.27)                | 15                     |
| Aspartate aminotransferase (IU/L)                                        | 21 (17–24)                     | 17                     |
| Alanine aminotransferase (IU/L)                                          | 17 (12–24)                     | 17                     |
| Blood urea nitrogen (mg/dL)                                              | 10 (8–11)                      | 17                     |
| Creatinine (mg/dL)                                                       | 0.84 (0.66–0.98)               | 17                     |
| Spirometric results                                                      |                                |                        |
| Forced expiratory volume in 1 s/forced vital capacity ratio              | 76.0 (62–82)                   | 15                     |
| % predicted forced expiratory volume in 1 s                              | 87.0 (67–100)                  | 15                     |
| % predicted forced vital capacity                                        | 86.0 (72–97)                   | 15                     |

*Data represent median (IQR) or number of patients (%).
level > 50 ppb was considered indicative of eosinophilic inflammation and responsiveness to corticosteroids in symptomatic patients and an increase over 10 ppb suggested a significant \( \Delta \text{FeNO} \) value [13].

**Treatment**

The parameters except FeNO level were used to tailor the corticosteroid treatment. The initial regimen for patients with newly diagnosed or uncontrolled CEP was 0.5 mg/kg/day of prednisolone. The dose was gradually tapered according to the clinical state. Patients with controlled CEP generally received a maintenance dose of 2.5- to 5-mg prednisolone daily. If no exacerbation event occurred during 3 months of maintenance treatment, the medication was discontinued. If symptom aggravation, reappearance of radiopacities, and peripheral eosinophilia were noted, suggestive of uncontrolled CEP, the dosage was increased up to 0.5 mg/kg/day.

**Statistical analysis**

Data are presented as median (interquartile range [IQR]) values or number (%) of patients. FeNO levels and peripheral eosinophil counts or percentages were analyzed with Pearson correlation analysis. Continuous variables were analyzed by using the Mann–Whitney \( U \)-test. The Wilcoxon signed-rank test was used to evaluate parametric differences during an exacerbation event and after corticosteroid administration. Receiver operating characteristic (ROC) curve analysis was used to determine the parametric values that best predicted exacerbation of CEP. \( P < 0.05 \) was considered to be statistically significant. All analyses were performed by using SPSS for Windows (version 18.0, SPSS, Inc., Chicago, IL, USA).

**Results**

**Baseline characteristics**

Eighteen patients (10 men) were enrolled in the study; fifteen patients had been diagnosed before the study began. The median age was 56 (41–68) years (Table 1). One patient (5.6%) was a current smoker, and 17 patients (94.4%) had never smoked or had stopped smoking. The most common symptom was cough (\( n = 15 \)), followed by sputum production (\( n = 13 \)). One patient (5.6%) had a history of pulmonary tuberculosis. The median peripheral eosinophil percentage was 21.2% (11.6–42.3%) of the total leukocyte count and median peripheral eosinophil count was 1543 (771–4034) cells/\( \mu L \). Seven patients underwent BAL for diagnosis of CEP. The median eosinophil percentage in BAL fluid was 47% (15–65%).

**Clinical course**

Seven patients (38.9%) had controlled CEP throughout the study. Ten exacerbation events occurred in nine patients (50%), with one patient experiencing two episodes. In total, 74 FeNO measurements were obtained from the 18 patients, including 10 measurements during exacerbation events and three at diagnosis. Therefore, 13 FeNO measurements were obtained during uncontrolled CEP (Figure 1). Median time interval between patient visits was 56 days (IQR 28–77). Median number of visits that were attended by the patients was 4 (IQR 4–5).

**Relationship of FeNO and peripheral eosinophilia**

The median FeNO value, peripheral eosinophil percentage, and peripheral eosinophil count were 37 (11–165) ppb, 5.1% (0.0–32.7%), and 283 (0–1938) cell/\( \mu L \), respectively. FeNO level was positively but weakly correlated with peripheral eosinophil percentage (\( r = 0.362, P = 0.003 \)) and count (\( r = 0.341, P = 0.005 \)). \( \Delta \text{FeNO} \) was positively and moderately correlated with \( \Delta \text{eosinophil percentage} \) (\( r = 0.695, P < 0.001 \)) and \( \Delta \text{eosinophil count} \) (\( r = 0.699, P < 0.001 \)) (Figure 2).

**Relationship of FeNO and clinical state**

The median FeNO levels were 79 (41–88) and 35 (26–49) ppb in uncontrolled (13/74 measurements) and controlled (61/74 measurements) CEP, respectively, showing a significant difference between the clinical states (\( P = 0.010 \)).
The median peripheral eosinophil percentage was also higher in the uncontrolled state (17.5% [10.8–22.3%] vs. 3.8% [1.6–6.5%]; *P* < 0.001). The peripheral eosinophil count showed a similar result (1239 [569–1608] cells/μL vs. 250 [110–389] cells/μL; *P* < 0.001) (Figure 3).

In nine of the 10 exacerbation events, FeNO level was measured after corticosteroid administration. The median FeNO level significantly decreased after the treatment (81 [67–95] ppb vs. 37 [32–44] ppb; *P* = 0.004). In five events, FeNO level was measured both before and after the episode. Significant changes in FeNO level was noted according to the clinical state of CEP (*P* = 0.022) (Figure 4).

There is one current smoker. His FeNO was measured after one hour cessation of smoking according to previous recommendation because smoking may decrease FeNO level [18,19]. His FeNOs were measured two times in stable state (29 and 33 ppb) which were within controlled state IQR (26–49).

![Figure 2 Relationship of FeNO level and peripheral eosinophilia in CEP.](image)

Scattergrams of FeNO level against peripheral eosinophil percentage (A) and count (B) as well as ΔFeNO against Δeosinophil percentage (C) and Δeosinophil count (D) at every assessment point are shown.
Diagnostic accuracy of FeNO
The area under the curve (AUC) of FeNO level was 0.835 (95% confidence interval = 0.716–0.954). At the cutoff level of 66 ppb, the sensitivity and specificity were 0.80 and 0.84, respectively. Further, the AUC of ΔFeNO was 0.918; at the cutoff value of 8.4 ppb, the sensitivity and specificity were 0.83 and 0.84, respectively (Figure 5 and Table 2). With regard to the ATS guidelines [20], the sensitivity and specificity at the 50-ppb cutoff level were 0.80 and 0.77, respectively, and those at the 10-ppb cutoff level of ΔFeNO were 0.67 and 0.86, respectively (Table 2).

The peripheral eosinophil percentage of 8.4% showed the best sensitivity (0.89) and specificity (0.79) for predicting exacerbation of CEP (AUC = 0.906). Further, the peripheral eosinophil count of 451 cells/μL was the best cutoff value (AUC = 0.923; sensitivity = 0.89; specificity = 0.83) (Figure 5 and Table 2).
Discussion

In this study, we evaluated FeNO as a potential marker of eosinophilic parenchymal inflammation and the clinical course of CEP. We found a moderate positive correlation between FeNO level and the degree of peripheral eosinophilia. Uncontrolled CEP was associated with a significantly higher FeNO level, and FeNO level increased during exacerbation events and decreased after corticosteroid treatment. To the best of our knowledge, this is the first study of FeNO in patients with CEP.

There are no clear diagnostic criteria for CEP. Most authors do not recommend histopathologic proof for establishing the diagnosis. Its diagnosis is based on suggestive clinical features, characteristic radiographic appearance, and peripheral eosinophilia [1,3,21]. We applied the Marchand et al. [1] criteria in this study. BAL fluid analysis may be helpful in diagnosis but is not a prerequisite for diagnosis of CEP. In some ways, it is more useful because the measurement method is completely noninvasive and easy to apply, and results are obtained immediately [20]. Moreover, the handheld FeNO monitor has the advantage of home-based use [27].

The FeNO level of 66.0 ppb showed the largest AUC with high sensitivity and specificity for predicting exacerbation of CEP. This value is near the ATS-recommended cutoff level (>50 ppb) [20], which also showed good sensitivity (80%) and specificity (77%). To account for each patient’s state of eosinophilic inflammation, we also evaluated ΔFeNO. The change in peripheral eosinophilia correlated well with ΔFeNO. Furthermore, the ΔFeNO value of 8.4 ppb showed good sensitivity and specificity for predicting exacerbation of CEP, similar to the ATS-recommended value of 10 ppb [20].

The present study has several limitations. First, all the FeNO measurements were combined because of the irregular assessment points in the small number of cases. However, the FeNO levels were simultaneously measured with the peripheral eosinophil and clinical parameters. Second, the 1-year follow-up duration is not enough to predict the long-term course of CEP. Third, the clinicians were aware of each patient’s FeNO levels, although they did not use them for tailoring the corticosteroid treatment. Fourth, FeNO levels of only three patients were measured at diagnosis of CEP. Additional FeNO data are needed to determine the cutoff value for diagnosis of CEP.

Table 2 Diagnostic validity of the studied parameters for exacerbation of CEP

| Variable                      | AUC     | Cutoff value | Sensitivity | Specificity |
|------------------------------|---------|--------------|-------------|-------------|
| FeNO level                   | 0.835   | 66.0 ppb     | 0.80        | 0.84        |
|                              |         | 50.0 ppb*    | 0.80        | 0.77        |
| ΔFeNO                        | 0.918   | 8.4 ppb      | 0.83        | 0.84        |
|                              |         | 10.0 ppb**   | 0.67        | 0.86        |
| Peripheral eosinophil percentage | 0.906   | 8.4%         | 0.89        | 0.79        |
| Peripheral eosinophil count  | 0.923   | 451 cells/μL | 0.89        | 0.83        |

*FeNO level > 50 ppb is indicative of eosinophilic inflammation and corticosteroid responsiveness in symptomatic patients [20].
**ΔFeNO > 10 ppb indicates significant increase in FeNO level [20].

Figure 5 ROC curves of the studied parameters for predicting exacerbation of CEP. ROC curves of FeNO level (black solid line), ΔFeNO (gray solid line), peripheral eosinophil percentage (black dotted line), and peripheral eosinophil count (gray dashed-dotted line) are shown.
Fifth, this retrospective study was conducted at a single center. Prospective multicenter clinical trials are required to analyze the association of symptoms, peripheral eosinophilia, and FeNO.

Conclusions
FeNO may be a useful marker for monitoring eosinophilic parenchymal inflammation and determining the appropriate corticosteroid dose in CEP.

Abbreviations
AEP: Acute eosinophilic pneumonia; AUC: Area under the curve; BAL: Bronchoalveolar lavage; CEP: Chronic eosinophilic pneumonia; FeNO: Fractional exhaled nitric oxide; IQR: Interquartile range; ppb: Parts per billion; ROC: Receiver operating characteristic.

Competing interests
The authors declare that they have no competing interests.

Authors’ contributions
JYP developed the study design, measured FeNO levels, analyzed the data, and drafted and revised the manuscript. TL, HYL, YJ, JSP, YIC, HIY, and JHL selected and followed the patients and critically read the paper. CTL conceived the study, developed the study design, collected the data, and drafted and revised the manuscript. All the authors read and approved the final manuscript.

Received: 5 April 2014 Accepted: 6 May 2014
Published: 12 May 2014

References
1. Marchand E, Reynaud-Gaubert M, Lauerque D, Durieu J, Tonnell AB, Cordier JF: Idiopathic chronic eosinophilic pneumonia. A clinical and follow-up study of 62 cases. The Groupe d’Etudes et de Recherche sur les Maladies “Orphelines” Pulmonaires (GERM’O’P). Medicine (Baltimore) 1998, 77(5):299–312.
2. Naughton M, Fahy J, Fitzgerald MX. Chronic eosinophilic pneumonia. A long-term follow-up of 12 patients. Chest 1993, 103(4):162–165.
3. Alam M, Burki NK. Chronic eosinophilic pneumonia: a review. South Med J 2007, 100(1):49–53.
4. Oh MJ, Lee JY, Choi DC. Exhaled nitric oxide measurement is useful for the exclusion of nonasthmatic eosinophilic bronchitis in patients with chronic cough. Chest 2008, 134(5):990–995.
5. Belytschko GS, Paranponaran K, Karnada D, Ethirimadis A, Hargreave FE: A comparison of exhaled nitric oxide and induced sputum as markers of airway inflammation. J Allergy Clin Immunol 2000, 106(4):638–644.
6. Payne DN, Adcock IM, Wilson NM, Oates T, Scallan M, Bush A: Relationship between exhaled nitric oxide and mucosal eosinophilic inflammation in children with difficult asthma, after treatment with oral prednisolone. Am J Respir Crit Care Med 2001, 164(3):Pt 1:1376–1381.
7. Warke TJ, Fitch PS, Brown V, Taylor R, Lyons JD, Ennis M, Shields MD: Exhaled nitric oxide correlates with airway eosinophilia in childhood asthma. Thorax 2002, 57(5):383–387.
8. Knuffman JE, Sorkness CA, Lemanske RF Jr, Mauger DT, Boehmer SJ, Martinez FD, Bacharier LB, Strunk RC, Szefleri SJ, Zeiger RS, Tausig LM: Phenotypic predictors of long-term response to inhaled corticosteroid and leukotriene modifier therapies in pediatric asthma. J Allergy Clin Immunol 2011, 128(1):41–47.
9. Smith AD, Cowan JO, Brassett KP, Fictell S, McLachlan C, Monti-Sheehan G, Herbison GP, Taylor DR: Exhaled nitric oxide: a predictor of steroid response. Am J Respir Crit Care Med 2005, 172(4):453–459.
10. Donohue JE, Jain N: Exhaled nitric oxide to predict corticosteroid responsiveness and reduce asthma exacerbation rates. Respir Med 2013, 107(7):943–952.
11. Michalis D, Baldassarre S, Van Myullem A: Exhaled nitric oxide and asthma control: a longitudinal study in unscreened patients. Eur Respir J 2008, 31(3):539–546.
12. Pettsky HL, Cates CJ, Lasserson TJ, Li AM, Turner C, Kynaston JA, Chang AB: A systematic review and meta-analysis: tailoring asthma treatment on eosinophilic markers (exhaled nitric oxide or sputum eosinophils). Thorax 2012, 67(3):199–208.
13. Smith AD, Cowan JO, Brassett KP, Herbison GP, Taylor DR: Use of exhaled nitric oxide measurements to guide treatment in chronic asthma. N Engl J Med 2005, 352(21):2163–2173.
14. Guo FH, de Ravee HR, Rice TW, Stuehr DJ, Thunnissen FB, Ezurum SC: Continuous nitric oxide synthesis by inducible nitric oxide synthase in normal human airway epithelium in vivo. Proc Natl Acad Sci U S A 1995, 92(17):7809–7813.
15. Lee JE, Rhee CK, Lim HJ, Lee SM, Shim YS, Lee CT, Lee SW: Fraction of exhaled nitric oxide in patients with acute eosinophilic pneumonia. Chest 2012, 141(5):1267–1272.
16. Cho YJ, Lim HJ, Park JS, Lee JH, Lee CT, Yoon H: Measurement of fractional exhaled nitric oxide in stable bronchiectasis. Tuberc Respir Dis 2013, 74(1):7–14.
17. American Thoracic Society, European Respiratory Society: ATS/ERS recommendations for standardized procedures for the online and offline measurement of exhaled lower respiratory nitric oxide and nasal nitric oxide, 2005. Am J Respir Crit Care Med 2005, 171(8):912–930.
18. Travers J, Marsh S, Aldington S, Williams M, Shrivillife P, Pitchard A, Weatherall M, Beasley R: Reference ranges for exhaled nitric oxide derived from a random community survey of adults. Am J Respir Crit Care Med 2007, 176(3):238–242.
19. Sandrin A, Taylor DR, Thomas PS, Hayes DHT: Fractional exhaled nitric oxide in asthma: an update. Respirology 2010, 15(1):77–80.
20. Dweik RA, Boggi PB, Ezurum SC, Ivirn CG, Leigh MW, Lundberg JO, Olin AC, Plummer AL, Taylor DR: An official ATS clinical practice guideline: interpretation of exhaled nitric oxide levels (FENO) for clinical applications. Am J Respir Crit Care Med 2011, 184(5):602–615.
21. Durieu J, Wallaret B, Tonnell AB. Long-term follow-up of pulmonary function in chronic eosinophilic pneumonia. Groupe d’Etude en Pathologie Interstitielle de la Societe de Pathologie Thoracique du Nord. Eur Respir J 1997, 10(2):286–291.
22. Barreto M, Villa MP, Monti F, Bohmova Z, Martella S, Montesano M, Darder MT, Ronchetti R: Additive effect of eosinophilia and atopy on exhaled nitric oxide levels in children with or without a history of respiratory symptoms. Pediatr Allergy Immunol 2005, 16(1):52–58.
23. Strunk RC, Szefleri SJ, Phillips BR, Zeiger RS, Chinchiilli VM, Larzen G, Hodgdon K, Morgan W, Sorkness CA, Lemanske RF Jr: Relationship of exhaled nitric oxide to clinical and inflammatory markers of persistent asthma in children. J Allergy Clin Immunol 2003, 112(3):883–892.
24. Fitzpatrick AM, Gaston BM, Ezurum SC, Teague WG: Features of severe asthma in school-age children: Atopy and increased exhaled nitric oxide. J Allergy Clin Immunol 2006, 118(1):1218–1225.
25. Jones SL, Kittelson J, Cowan JO, Flanneny EM, Hancock RJ, McLachlan CR, Taylor DR: The predictive value of exhaled nitric oxide measurements in assessing changes in asthma control. Am J Respir Crit Care Med 2001, 164(3):738–743.
26. Szefleri SJ, Wenzel S, Brown R, Ezurum SC, Fahy JV, Hamilton RG, Hunt JF, Kita H, Liu AH, Panettieri RA Jr, Schleimer RP, Minicuzzi MD: Asthma outcomes: biomarkers. J Allergy Clin Immunol 2012, 129(3 Suppl):59–523.
27. Kapande KM, McConaghy LA, Douglas I, McKenna S, Hughes JI, McCance DR, Ennis M, Shields MD: Comparative repeatability of two handheld fractional exhaled nitric oxide monitors. Pediatr Pulmonol 2012, 47(6):546–550.

DOI:10.1186/1471-2466-14-81
Cite this article as: Park et al.: Significance of fractional exhaled nitric oxide in chronic eosinophilic pneumonia: a retrospective cohort study. BMC Pulmonary Medicine 2014 14:81.