Subtypes of Severe Asthma Based on A Combination of Blood Eosinophil Counts and Levels of Exhaled Nitric Oxide

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Rationale

1) Patients with severe asthma (SA) has been provided with clinical benefit according to classification based on blood eosinophil counts (bl-Eos).

Blood eosinophil ≥400/µL is likely • a risk factor of severe exacerbation. • adjusted RR 1.31 (Zeiger RS, et al. JACI Pract 2014;2:741-50)

• a predictive marker of sputum eosinophilia. (Fowler SJ, et al. JACI 2015;136:822-24)

2) Exhaled nitric oxide (FENO) is a major predictive marker for eosinophilic airway inflammation. High levels of FENO also seem to represent Type 2 airway inflammation because of their production by IL-4/13.

✓ FENO is recognized as a surrogate marker of eosinophilic airway inflammation. (Dweik RA, et al. AJRCCM. 2011;184:602-15.)

Objective

The objective of this study is to address phenotypes of severe eosinophilic asthma based on the classification by the combination of FENO as a biomarker of type 2 airway inflammation and b-Eos as a biomarker of potent systemic eosinophilic inflammation.

Methods

Subjects

Eligible patients were: 1) ≥ 20 years old coming to our outpatient clinic section. 2) Diagnosed as severe asthma based on Japanese guidelines for adult asthma 2017 (Allergol Int. 2017;66:163-189).

Methods

1) A cross-sectional observational study

2) The data was extracted from outpatient medical record for a year beginning from the day bloods were obtained.

Measurements

✓ Medical record: age, sex, BMI, smoking history, sensitization to allergens, allergic comorbidities, medication, acute exacerbation history

✓ Blood: b-Eos, total IgE, FENO, Pulmonary function

Classification

Eligible patients were divided into 4 subgroups defined by the following cutoffs for FENO values (ppb) and b-Eos counts (cells/mm^3).

• Low FENO and low b-Eos: FENO < 38 and b-Eos < 300
• High FENO and low b-Eos: FENO ≥ 38 and b-Eos < 300
• Low FENO and high b-Eos: FENO < 38 and b-Eos ≥ 300
• High FENO and high b-Eos: FENO ≥ 38 and b-Eos ≥ 300

Cutoff values were decided by identifying the optimal cut-off value for sputum eosinophils ≥ 3% with the use of receiver operating characteristic curve (ROC) analysis.

The optimal cut-off values of FENO and b-Eos for sputum eosinophil ratios ≥ 3%

The ROC for individual FENO values and b-Eos counts to differentiate between sputum eosinophil <3% and ≥3%

Correlation of sputum eosinophil ratios with FENO and b-Eos counts

FENO: 37 45.0% 100%

b-Eos: 76.5% 71.4%

Sputum eosinophil ratio vs FENO

Sputum eosinophil ratio vs b-Eos counts

The optimal cut-off values FENO 38ppb

★ Bi-Eos 300/µL

Conclusions

✓ The classifications of SA based on airway and systemic type 2 inflammation biomarker demonstrated features of SAs.

✓ SAs with high FENO and b-Eos exhibited frequent severe asthma exacerbations, higher prevalence of chronic sinusitis and lower %FVC.

✓ SAs with both high type 2 inflammation biomarkers are consistently under unstable condition despite of guideline therapy.

COI Disclosure

Name of first author: Hidetoshi Iemura

The presenters have no financial conflicts of interest to disclose concerning the presentation.