Eosinopenia as a Marker of Outcome in Acute Exacerbations of Chronic Obstructive Pulmonary Disease

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\textbf{ABSTRACT}

\textbf{Background:} Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is a common cause of hospitalization and mortality. Recent studies have shown the usefulness of eosinopenia in predicting the outcomes of patients admitted to the intensive care unit. This study examined the association of eosinopenia with the outcomes of patients with AECOPD.

\textbf{Methods:} This is a prospective study. Patients with AECOPD were divided into two cohorts: patients with eosinopenia and those without eosinopenia. Duration of hospitalization, need of mechanical ventilation, in-hospital mortality, rehospitalization, or death within 30 days after discharge were compared between the two cohorts. Eosinopenia was defined as eosinophil count of $>40$ cells/mm\textsuperscript{3}.

\textbf{Results:} Among 100 patients with AECOPD, 44 were eosinopenic and 56 were non-eosinopenic. Duration of hospitalization of patients with eosinopenia was $12.38 \pm 9.85$ days and that of patients without eosinopenia was $7.35 \pm 5.68$ days ($p = 0.001$). In all, 16 (36\%) patients with eosinopenia and seven (12\%) patients without eosinopenia needed mechanical ventilation ($p = 0.005$). In-hospital mortality rate among eosinopenic and noneosinopenic patients was 37.5\% (12/44) and 7.6\% (4/56), respectively ($p = 0.006$). Among 100 patients with AECOPD, 16 died in the hospital. Of these, 12 (27.27\%) were eosinopenic and 4 (7.6\%) were noneosinopenic ($p = 0.006$). The mean eosinophil count of patients who died in the hospital ($n = 16$) was 44.00 cells/ml whereas that of survivors ($n = 84$) was 107.41 cells/ml ($p = 0.022$).

\textbf{Conclusion:} We conclude that a significant relationship exists between eosinopenia and outcomes of patients with AECOPD. Thus, eosinopenia can be a useful, easy-to-measure, and inexpensive biomarker for predicting the prognosis of patients with AECOPD.

\textbf{Keywords:} COPD, eosinopenia, outcome, mortality, duration of hospitalization
INTRODUCTION

Global Initiative for Chronic Obstructive Lung Disease (GOLD) stated that chronic obstructive pulmonary disease (COPD) is the fourth leading cause of death in the world and is going to be the third cause of death by 2020 (1, 2). The American Thoracic Society (ATS) and the European Respiratory Society (ERS)(3) stated that although this disease mainly involves the lungs it has specific systemic complications with increase in systemic inflammatory markers (4, 5).

Acute exacerbations of COPD (AECOPD) has a 10% mortality rate at admission and one third of the patients die within a year after hospitalization (6).

Some biomarkers were studied for prediction of outcomes in AECOPD. However, there is little information about the real relationship between para-clinical markers and clinical outcomes like duration of hospitalization, need to intensive care and mortality (7-9). Some biological and hematological parameters such as copeptin, C-reactive protein (including hs-CRP), and procalcitonin, have been used to determine the prognosis in AECOPD (8, 10). Although these tests helped to find out that COPD is a systemic disease, these tests are not available in every medical centers and require extra-cost.

The simplest test which is usually ordered for every admitted patient is a complete blood count (CBC). In this test eosinophilia is identified as a marker of allergy and parasitic disease, but recently, eosinopenia was showed as a sensitive and specific marker for sepsis in intensive care unit (ICU) patients (11). It is recently used for prediction of prognosis in adult (12) and pediatric (13) ICUs. In addition, there are studies that reported occurrence of eosinopenia after burning or injury which lasts up to a few days (14-16).

In this study, we aimed to evaluate the usefulness of eosinopenia for prediction of outcomes in AECOPD.

MATERIALS AND METHODS

This study was performed in Imam Khomeini hospital of Urmia, Iran. It was approved by ethical committee of Urmia University of Medical Science.

Patients who hospitalized because of AECOPD were enrolled into two cohorts according to admission day CBC, with eosinopenia and without eosinopenia. We excluded the patients who used systemic corticosteroids during the last 30 days, patients with asthma, new infiltration on chest X-ray during hospitalization, heart failure, and other diseases that could change the level of eosinophils.

A physician not in charge of patient’s management collected the data and followed the course of treatment and outcomes. Data like sex, age, smoking, white blood cell (WBC) count, pH of arterial blood sample and spirometry were recorded. Outcome parameters such as duration of hospitalization, mechanical ventilation and death in hospital were collected. Discharged patients were followed up by phone after 30 days about poor outcomes (mortality and re-hospitalization).

Data were analyzed by SPSS software (Chicago, version 18. USA). T-test is used to compare means. Mortality and re-hospitalization after discharge were compared with using Fisher’s exact test. P value less than 0.05 was considered statistically significant.

Eosinopenia was defined as eosinophil count less than 40/mm³ on admission day. COPD diagnosis was based on GOLD criteria (1) and the diagnosis of AECOPD was based on acute increase of dyspnea, cough and sputum, and sputum purulence severe enough to require medical care in hospital (17).

RESULTS

One hundred patients with AECOPD (44 with eosinopenia and 56 without eosinopenia) were evaluated. Table 1 shows characteristics and outcomes of the two groups. There was no significant differences between the two groups for sex, age, current smoking, WBC count, arterial pH, and spirometric data (p value for all variables >0.05).

There were significant differences in outcomes (death in hospital, need for mechanical ventilation, and duration of hospitalization) between the two cohort groups with p value for all variables less than 0.05).

Within 30 days after discharge, 9 (28%) of 32 discharged eosinopenic group were re-hospitalized for AECOPD and four of them were died, while only two (3.57%) of the patients with normal eosinophil count needed hospitalization again and one of them died (p value: 0.04).
DISCUSSION

Our findings showed that eosinopenia had a significant relationship with duration of hospitalization, need for mechanical ventilation, and death in the hospital, re-hospitalization and mortality within 30 days after discharge in patients with AECOPD.

Eosinophils consist of 0-7% of peripheral blood cells and its production is regulated by granulocyte–macrophage colony-stimulating factor, interleukin-3 and interleukin-5 (18, 19).

Clinicians consider eosinophilia for suspicion of allergic and parasitic disease. Infectious and non-infectious stimuli of acute inflammation markedly suppress eosinophilia. Decrease in eosinophil count during sepsis and inflammatory process is because of destruction of the cells in peripheral tissues, suppression of the migration of mature eosinophils from the bone marrow, localization in inflammatory sites and suppression of formation in bone marrow (19).

Eosinopenia also occurs with acute stress, which is mediated by adrenal glucocorticoids and epinephrine (20).

Relation between eosinopenia and poor prognosis and mortality of patients may be related to the presence of bacterial infections, and eosinopenia is a marker of infection. Abidi et al (12) showed that there was a strong relationship between bacterial infection and eosinopenia in severe patients. They suggested that eosinopenia could differentiate between sepsis and inflammatory response. Others suggested that eosinopenia is more predictive of death than of an infection because it can develop from acute severe stress of infectious or noninfectious, both of which are associated with mortality (13, 21).

Although, some studies like the study of Smithson et al (22) could not find a relation between eosinopenia and infection in intensive care units. Setterberg et al (23) indicated that lack of eosinophil in the peripheral blood sample could not be a valuable marker of infection.

To our knowledge and search in accessible data bases, only one study by Holland et al (24) evaluated the value of eosinopenia in AECOPD. They studied 65 patients with AECOPD, 42 patients with normal eosinophil count and 23 patients with eosinopenia, and showed a significant relationship between eosinopenia and duration of hospitalization and mortality. They indicated that eosinophil count was an
independent marker to determine the severity of disease in patients with AECOPD. However they stated that their study was retrospective and they had no information about receiving corticosteroid, so decrease in eosinophil count could be due to corticosteroids effect. In our prospective study, we excluded the patients that had received systemic corticosteroid, so systemic corticosteroids cannot act as confounding factor.

**CONCLUSION**

Eosinophil count could be a useful easy-to-measure, inexpensive biomarker to determine the severity and predict the prognosis of patients with acute exacerbation of COPD.

Conflict of interests: none declared.

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**REFERENCES**


