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Original Article

Association between blood eosinophil count with asthma hospital readmissions[☆]

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ABSTRACT

Introduction: The presence of eosinophils in asthma inflammation is a relevant factor in the pathophysiology of the disease, however the relationship between the blood eosinophil count (BEC) with asthma severity and prognosis is still under debate.

The aim of this work is to analyze the relationship between the BEC levels and hospital readmissions in patients with asthma.

Material and methods: A review was retrospectively carried out on all admissions of patients over 18 years old due to exacerbation of asthma occurring in our hospital between the years 2000 and 2010. The personal characteristics and the asthma personal history of each patient were recorded. The BEC was determined from the first blood sample taken from the patient after their arrival at the hospital. Hospital early, late and frequent readmissions were analyzed using 4 cut-off points; less than 150 eosinophils/μL vs \geq 150/μL, less than 200 vs v200 /μL, less than 300 vs \geq 300/μL, and less than 400 vs \geq 400/μL.

Results: We have included 1316 patientsy, 70% of whom are women, as well as a mean age of 60 years, and a mean FEV1 of 73.5% of the reference value. The mean eosinophil blood count was 201.7 cells/ μ L. A BEC \geq 300 cells/ μ L showed a reduction of risk of late readmission of 42%, a BEC \geq 400 cells/ μ L showed a reduction in late readmission risk of 41% and decrease in frequent late readmission of 63%.

Conclusions: Our study appears to support that an elevated BEC is associated with a lower incidence of asthma hospital readmissions.

1. Introduction

Asthma is a heterogeneous disease in which the pathophysiology interacts with genetic and environmental factors [1]. The presence of eosinophils in asthma inflammation has been known for many years to be a relevant factor in the pathophysiology of the disease [2] and has

demonstrated its use as a biomarker in the identification of patients with an improved response to some treatments [3,4].

It has been known since the end of the 1950's that the sputum eosinophil count (SEC) is a predictor of the response to treatment with corticosteroids [5]. However, eosinophils are not a marker of severity in all asthmatic patients. Thus, when Wenzel et al., analyzed the bronchial

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biopsies of patients with severe asthma refractory to corticosteroids, they observed eosinophilia in approximately half of these patients, while in the rest the presence of eosinophils was very limited [6].

Since then, interesting studies have been carried out to determine the usefulness of eosinophils in the management of asthma, but the controversy persists.

The studies available seem to support that the SEC levels are associated with more severe asthma or with a poorer outcome of the disease [7-10].

However, the data on the blood eosinophil count (BEC) are more discrepant. Thus, some authors report that the BEC do not correlate with the severity of the asthma [7,8], while other authors observed that the patients with a high BEC have more severe asthma [11,12]; or on the contrary, patients with a high BEC are associated with less severe exacerbations [13].

The greater usefulness of SEC levels has not been reflected in all the studies, since in one recent publication, on analyzing the response to mepolizumab in severe eosinophilic asthma, it was observed that the BEC was a better predictor of response than the SEC [14].

On the other hand, the determination of SEC is a particularly complex technique and of high cost. Thus, it is not available in all health centers, as such that other methods have been explored for identifying the eosinophilic phenotype, such as the determination of the fraction of exhaled nitric oxide, periostin levels in serum, or the BEC [15].

Given that the BEC determination is widely available, and is cheaper than the sputum analysis, it could be used as a more effective indicator in the management of asthma.

Hospital admissions account for a significant part of the health care costs of asthma, as well having a high impact on the quality of life of the patients and their families [16–18]. In Spain, a slight downward trend is observed in the mortality due to asthma [19], although hospital admissions continue to increase, particularly in elderly women [20].

Hospital readmissions may be a good indicator of the quality of the health care, as well as a potential target for reducing health care costs [21–23].

The aim of this work is to analyze the relationship between the BEC levels and hospital readmissions in patients with asthma.

2. Material and methods

A review was retrospectively carried out on all admissions of patients over 18 years old due to exacerbation of asthma occurring in our hospital between the years 2000 and 2010. The data were gathered by two members of the research team whilst reviewing the clinical records. In cases where there were discrepancies in the evaluation of any data, the decision was made by consensus with the rest of the group members. The definition of asthma exacerbation was based on the discharge report produced by the specialist doctor who treated the patients (pulmonlogists or internists), with review of medical records by our research team (including pulmonologists, internists, and radiologists).

Cases where the reason was due to another specific cause, such as pulmonary embolism or pneumonia, were excluded.

The personal characteristics of each patient were recorded including age (categorized into 4 groups: from 18 to 35 years, from 36 to 55 years, from 56 to 75 years, and > 75 years), gender, body mass index (BMI), classifying the patients into normal weight when they had a BMI less than 25 kg/m², as overweight with a BMI greater than or equal to 25, and a BMI greater than or equal to 30 as obese [24]. Comorbidity was evaluated according to the Charlson index [25], and smoking classified as active smokers, ex-smokers, or never smoked.

An analysis was performed on the asthma personal history, including the baseline treatment, lung function based on the forced

expiratory volume (FEV1) as a percentage of the reference value, the baseline severity of the asthma according to the Global Initiative for Asthma (GINA) 2006 criteria [26], having had any hospital emergency department (ED) visits or admissions due to asthma in the previous year. As regards the exacerbation index, the duration of hospital stay was analyzed (including from the time the patient arrived in the ED until discharge), and treatment after hospital discharge.

Previous year emergencies were stratified into 3 groups, one group with those who did not make any visit to the ED in the previous year, another that made one to three visits, and a last group that made four or more visits to the ED in the previous year. Previous year hospital admissions were stratified into 3 groups, one group with those who did not have any hospital admission in the previous year, another that had one hospital admission, and a last group that had two or more hospital admissions in the previous year.

The BEC was determined from the first blood sample taken from the patient after their arrival at the hospital. Hospital readmissions were analyzed using 4 cut-off points; less than 150 eosinophils/ μ L vs \geq 150/ μ L, less than 200 vs v200/ μ L, less than 300 vs \geq 300/ μ L, and less than 400 vs \geq 400/ μ L [9,12,27,28].

An early readmission (ER) was defined as that which occurred in the following 15 days after hospital discharge, and late readmission (LR) as that occurring from 16 days after discharge [22]. In order to analyses the LR, those that had no LR were compared with those that had any LR. For the evaluation of the relationship with the patients frequent late readmissions (FLR), those that had no LR were compared with those that had had two or more LR during the study period.

The hospital stay included from the time the patient arrived in the ED until discharge.

The Review Board on Human Studies at our institution approved the protocol (**Register Code**: 2017/093).

2.1. Statistical analysis

The data were tested for normal distribution using the Kolmogorov-Smirnov test. The comparison of the categorical variables was performed using the Chi-squared test.

The variables with significant differences in the univariate analysis were included in the multivariate analysis using logistic regression. The Odds Ratios (OR) of a higher incidence of ER and LR were calculated using a binary logistic regression, including blood eosinophil count, gender, and treatment after hospital discharge with combinations of inhaled corticosteroids and long acting beta-agonists (ICS-LABA), inhaled, or oral corticosteroids, as independent variables.

All statistical analyses were performed using SPSS 15.0 for Windows, Version 15.0 (SPSS Inc., Chicago, Illinois, USA).

3. Results

We have included 1316 patients in our study, 70% of whom are women, as well as a mean age of 60 years, and a mean FEV1 of 73.5% of the reference value. The mean eosinophil blood count was 201.7 cells/ μL (Table 1). The main characteristics of included patients according to the BEC are shown in Table 2.

Readmission data were collected from 1170 patients. Of these, there was early readmission (ER) in 17 (1.4%) patients, a late readmission (LR) in 241 (21%) patients, and two or more late readmissions in 74 (6%) patients (Table 3).

A BEC of 400 or more cells/ μL was found in 16% of the patients, with 23% with 300 or more cells/ μL (Table 3).

On analyzing the correlation between the different BEC levels in which the sample was stratified with the ER, we did not observe any significant relationship. A lower incidence of LR was observed in

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