

The impact of high peripheral blood eosinophil count during treatment of infective COAD exacerbation on the length of hospital stay and the rate of readmission

Ibrahim TM^{1,2*}, Abdullah Al-allawi¹ and Jaganaathan Srinivasan¹

¹Department of Medicine, Goulburn Valley Base Hospital, Graham Street Shepparton, Australia

²Clinical Rural School of Medicine, The University of Melbourne, Graham Street, Australia

Abstract

Background: Chronic obstructive airway disease (COAD) is a neutrophilic inflammatory disease but can transform into eosinophilic inflammation during exacerbation usually reflected in increase sputum eosinophil count. Peripheral blood eosinophilia (PBE) has been reported in some studies to be a good marker of sputum eosinophil. Eosinophilia either in the sputum or peripheral blood has also been reported to be associated with increased risk of infective exacerbation and increased response to inhaled corticosteroid (ICS) in patients with COAD. The aim of this study is to determine the relationship of post admission PBE counts and the outcomes in the treatment of acute infective exacerbation of COAD.

Methods: This is a prospective study of patients with COAD admitted with infective exacerbation between June to September 2016 and followed up till January 2017. The PBE of the patients were estimated on admission and on discharge. The patients were classified into eosinophilic and none-eosinophilic COAD on discharge based on the level of blood eosinophil count of above or below $0.3 \times 10^9/l$ respectively. Means and student t test were used to describe the none categorical data and odd ratio (OR) was used to determine the risk of readmission.

Results: On admission 26.7% (16) had eosinophilic COAD (mean PBE count of $0.545 \times 10^9/l \pm 0.339 \times 10^9/l$) while 73.3% (44) had none-eosinophilic COAD ($0.0454 \times 10^9/l \pm 0.0663 \times 10^9/l$). There was no difference in the length of hospital stay (LOHS) between patients with PBE count of $\geq 0.3 \times 10^9/l$ (5.36 ± 6.26 days) and those with $\leq 0.2 \times 10^9/l$ (6.26 ± 4.57 days) on admission ($t = -0.48848$, $p = 0.314$). Irrespective of the PBE on admission most of the patients (95.3%) received parenteral (oral or intravenous) corticosteroid as part of their treatment regimen. On discharge most patients (96.2%) had low mean PBE of $0.078 \pm 0.084 \times 10^9/l$ while only 3.8% had a mean PBE count of $0.400 \pm 0.141 \times 10^9/l$. Those with PBE of $\geq 0.3 \times 10^9/l$ on discharge are at a slightly higher risk of readmission than those with count of $\leq 0.2 \times 10^9/l$ with odd ratio of 1.7 (CI=95%). 50% of those with PBE $> 0.3 \times 10^9/l$ and 37.5% of those with count $\leq 0.2 \times 10^9/l$ were readmitted at least once during the study period. The prescription of ICS or lack of it on discharge does not have significant influence on the risk of readmission post treatment for AE/COAD with OR = 0.7 (CI=95%). Only 38.7% of those discharged on ICS and 64% of those who were not given ICS on discharge were re-admitted at least once in the study period.

Conclusion: The PBE count on admission had no significant impact on the LOHS and COAD Patients with PBE $\geq 0.3 \times 10^9/l$ at discharge post treatment for AE/COAD had marginal significant risk of at least one readmission in 6 months post discharge with OR of 1.7. While the use of ICS post discharge had no impact on the rate of readmission.

Introduction

COAD is a neutrophilic inflammatory disease but can transform into eosinophilic inflammation during exacerbation. This is usually reflected in increase sputum eosinophil count. Peripheral Blood Eosinophilia (PBE) has been reported to be a good marker of sputum eosinophil. And eosinophilia either in the sputum or peripheral blood has been reported to be associated with increased risk of acute infective exacerbation and increases response to inhaled corticosteroid (ICS) in patients with COAD [1-3]. The aim of this study is to determine the relationship of post admission PBE counts and the outcomes in the treatment of acute infective exacerbation of COAD.

Methods

This is a prospective study of patients with COAD admitted with infective exacerbation between June to September 2016 and followed up till January 2017. The PBE of the patients were estimated on admission and on discharge. The patients were followed up for between

3-7 months post discharge and the rate of readmission was recorded. The patients were classified into eosinophilic and none-eosinophilic COAD on discharge based on the level of blood eosinophil count of above or below $0.3 \times 10^9/l$ respectively. Means and student t test were used to analyze the none categorical data and odd ratio (OR) was used to determine the risk of readmission.

Results

On admission 95% of the patients were on ICS and 26.7% (16) had eosinophilic COAD (mean PBE count of $0.545 \times 10^9/l \pm 0.339 \times$

Correspondence to: Tunde Maiyaki Ibrahim, Department of Medicine, Goulburn Valley Base Hospital, Graham Street Shepparton, Victoria, Australia, E-mail: imaiyaki@yahoo.com

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Table 1. The relationship of blood eosinophil count and inhaled corticosteroid use to length of hospital stay and readmission rate.

PBE Count o+A20+A2:F20+A2+A2:F20	Proportion of patients		
$\geq 0.300 \times 10^9/L$	26.7% (n=11)		
$\leq 0.200 \times 10^9/L$	73.3% (N=45)		
Mean PBE Count on admission			
$0.545 \times 10^9/L \pm 0.339$	26.7% (N=11)	$t=8.43138, p=0.00001$	
$0.0454 \times 10^9/L \pm 0.0663$	73.3% (N=45)		
PBE Count on Admission	LOHS(days)		
$\geq 0.300 \times 10^9/L$	5.36 ± 6.26	$t=-0.48848, p=0.3141$	
$\leq 0.200 \times 10^9/L$	6.26 ± 4.57		
Mean PBE Count on discharge	Proportion(n)		
$0.400 \times 10^9/L$	3.77% (n=2)	$t=5.41391, p=00001$	
$0.078 \times 10^9/L$	96.23% (n=51)		
PBE count o discharge	Rate of re-admission		
$\geq 0.300 \times 10^9/L$	$\geq 50\%$ (n=1)	$0=50\%$ (n=1)	OR=1.7 (CI=95%)
$\leq 0.200 \times 10^9/L$	$\geq 37.5\%$ (n=21)	$0=62.5\%$ (n=35)	
ICS use on discharge	Readmission Rate (number/mths)	Ra (number/6mths)	
	≥ 1	0	
Used ICS (42)	38.10%	61.90%	OR=0.8 (CI=95%)
No ICS (16)	43.80%	56.20%	

$10^9/l$) while 73.3% (44) had none-eosinophilic COAD ($0.0454 \times 10^9/l \pm 0.0663 \times 10^9/l$). There was no difference in the length of hospital stay (LOHS) between patients admitted with PBE count of $\geq 0.3 \times 10^9/l$ (5.36 ± 6.26 days) and those with $\leq 0.2 \times 10^9/l$ (6.26 ± 4.55 days) on admission ($t=-0.48848, p=0.314$). Irrespective of their use of ICS and PBE on admission most of the patients (95.3%) received parenteral (oral or intravenous) corticosteroid as part of their treatment regimen. On discharge most patients (96.2%) had low mean PBE of $0.078 \pm 0.084 \times 10^9/l$ while only 3.8% had a mean PBE count of $0.400 \pm 0.14 \times 10^9/l$. Those with PBE of $\geq 0.3 \times 10^9/l$ on discharge are at a slightly higher risk of readmission than those with count of $\leq 0.2 \times 10^9/l$ with odd ratio of 1.7. 50% of those with PBE $>0.3 \times 10^9/l$ on discharge and 37.5% of those with count $\leq 0.2 \times 10^9/l$ were readmitted at least once during the study period. The prescription of ICS or lack of it on discharge does not have significant influence on the risk of readmission post treatment for AECOAD with OR = 0.8 (CI=95%). Only 38.7% of those discharged on ICS and 64% of those who were not given ICS on discharge were re-admitted at least once in the study period. Detail is summarized in table 1.

Discussion

Most of the patients (73.3%) admitted with AECOAD in this study had PBE of $0.078 \times 10^9/l$ on admission while only a small percentage (26.7%) had a high count of about $0.4 \times 10^9/l$. This is probably due to the use of ICS in most of the patients prior to their admission. The level of admission or discharge PBE had no significant impact on the LOHS. And the risk of readmission with AECOAD is only mannerly higher in those with PBE $\geq 0.3 \times 10^9/l$ on discharge than in those with a count of $\leq 0.2 \times 10^9/l$. This finding is like those reported in earlier studies relating PBE and other inflammatory biomarkers to frequency of exacerbation in patients with stable COAD [3-6]. But the association between the PBE and readmission risk in our study is only modest contrary to the findings reported in the study by Price et al. [4] 37% of patients with PBE $>0.5 \times 10^9/l$ had one or more exacerbation during the study period. Watz et al. [5] reported that increase PBE after withdrawing ICS is associated with increased frequency of exacerbation in patients with moderate-severe COAD and concluded that PBE of $\geq 300/ul$ (4%) not only increase the risk of exacerbation but also predict occurrence of deleterious consequences on withdrawal of ICS. Pavord et al. [7]

and Vedel-Krogh et al. [3] also found that increased PBE of more than 2% and $0.3 \times 10^9/l$, respectively are associated with significant increase in rate of exacerbation. Thomsen et al. [1] reported that the OR of exacerbation in COAD patients with elevated 3 bio-inflammatory markers (leucocytes, CRP and fibrinogen) is about 3.7 this is comparable to that found in this Study (OR=3.26). This study also revealed that the use of ICS post discharge after exacerbation has no significant effect on the risk of readmission. This is different from the findings reported by Pascoe et al. [6] and Pavord et al. [7] that the use of ICS is more effective in reducing risk of exacerbation in those patients with high level of blood eosinophil. The finding in this study even though is modest and strong findings in the earlier studies demonstrate that blood eosinophil count can be used in decision making during management of COAD exacerbation. More studies are needed to validate the post treatment cutoff PBE count target.

Conclusion

COAD Patients with PBE $\geq 0.3 \times 10^9/ul$ at discharge post treatment for infective exacerbation have a minimal risk of at least one readmission within 6 months post discharge but the admitting PBE had no impact on the LOHS.

References

- Thomsen M, Ingebrigtsen TS, Marott JL, Dahl M, Lange P, et al. (2013) Inflammatory biomarkers and exacerbations in chronic obstructive pulmonary disease. *JAMA* 309: 2353-2361. [Crossref]
- Negewo NA, McDonald VM, Baines KJ, Wark PA, Simpson JL, et al (2016). Peripheral blood eosinophils: a surrogate marker for airway eosinophilia in stable COPD. *Int J Chron Obstruct Pulmon Dis* 11: 1495-1504. [Crossref]
- Vedel-Krogh S, Nielsen SF, Lange P, Vestbo J, Nordestgaard BG (2016) Blood Eosinophils and Exacerbations in Chronic Obstructive Pulmonary Disease. The Copenhagen General Population Study. *Am J Respir Crit Care Med* 193: 965-974. [Crossref]
- Kerkhof M, Sonnappa S, Postma DS, Brusselle G, et al. (2017) Blood eosinophil count and exacerbation risk in patients with COPD. *Eur Respir J* 50. [Crossref]
- Watz H, Tetzlaff K, Wouters EF, Kirsten A, Magnussen H, et al. (2016) Blood eosinophil count and exacerbations in severe chronic obstructive pulmonary disease after withdrawal of inhaled corticosteroids: a post-hoc analysis of the WISDOM trial. *Lancet Respir Med* 4: 390398.

6. Pascoe S, Locantore N, Dransfield MT, Barnes NC, Pavord ID (2015) Blood eosinophil counts, exacerbations, and response to the addition of inhaled fluticasone furoate to vilanterol in patients with chronic obstructive pulmonary disease: a secondary analysis of data from two parallel randomised controlled trials. *Lancet Respir Med* 3: 435-442. [[Crossref](#)]
7. Pavord ID, Lettis S, Locantore N, Pascoe S, Jones PW, et al. (2016) Blood eosinophils and inhaled corticosteroid/long-acting β_2 -agonist efficacy in COPD. *Thorax* 71: 118-125. [[Crossref](#)]