Innate Pulmonary Response to Community-Acquired Pneumonia (CAP) in Patients with Chronic Obstructive Pulmonary Disease (COPD):

Results from the Community-Acquired Pneumonia Inflammatory Study Group (CAPISG)

Lisandra Rodriguez Hernandez, MD, MD1, Jorge Perez San Juan, MD, MD2, Robert R. Kelley, PhD, PhD, Timothy L. Wiemken, PhD, PhD3, Rafael Fernandez-Botran, PhD, PhD, Martin Gnoni, MD, MD4, Jose Bordon, MD, MD, PhD, MD5, Madhavi Rane, PhD, PhD6, Forest Arnold, DO, DO7, Julio A. Ramirez, MD8, and Silvia Urrutia, PhD9.

1Division of Infectious Diseases, University of Louisville, Louisville, KY, 2Pathology and Laboratory Medicine, University of Louisville, Louisville, KY, 3Department of Internal Medicine, Providence Hospital, Washington, DC, 4Division of Nephrology, University of Louisville, Louisville, KY, 5Kidney Disease Program, University of Louisville, Louisville, KY.

ABSTRACT

Patients with COPD have chronic airway inflammation characterized by increased cytokine levels and neutrophil activation. It is well defined if chronic inflammatory changes in the airways of patients with COPD result in an innate pulmonary response during a CAP. The objective of this study was to compare cytokine production and neutrophil function in patients with and without COPD.

Blood samples were collected from patients diagnosed with COP on admission to the hospital. The plasma levels of 10 different cytokines were measured by luminex, as well as the peripheral blood neutrophil function using flow cytometry (mfc). Patients were grouped according to the presence of COPD (CAP-COPD (+) vs. CAP+COPD (-)).

A total of 14 CAP-COPD (+) and 26 CAP+COPD (-) patients were enrolled. Median (interquartile range) CD35 expression was 163 (111) in CAP+COPD (-) and 127 (101) in CAP+COPD (+) (P<0.238). CD66b expression was 62 (44) in CAP+COPD (+) and 63 (24) in CAP+COPD (-) (P<0.847). Phagocytosis in Staphylococcus aureus was 837 (810) in CAP+COPD (+) and 913 (880) in CAP+COPD (-) (P<0.713). H2O2 production was 538 (480) in CAP+COPD (+) and 726 (406) in CAP+COPD (-) (P<0.494).

The innate pulmonary response during an episode of CAP measured by cytokine production and neutrophil function is not different in patients with or without COPD. These data support the clinical concept that COPD is not a risk factor to poor outcomes in patients with CAP.

INTRODUCTION

Community acquired pneumonia (CAP) and COPD are common cause of morbidity and mortality in adults. It is observed by the coexistence of both conditions, and there are a lot of studies trying to show their relationship, but the evidence on higher mortality risk with their association is weak and heterogeneous. (3)

Neutrophils play an important role in the pathophysiology of CAP and COPD. It is well known that neutrophils are critical for the resolution of pneumonia, being the first line of defense against bacterial infections. (4) On the other hand, neutrophils are considered to play a role in pathological processes that characterize COPD. (5) Patients with COPD have chronic airway inflammation characterized by increased cytokine levels and neutrophil activation. It is not well defined if chronic inflammatory changes in the airway may impair the innate pulmonary response during an episode of CAP. The objective of this study was to compare cytokine production and neutrophil function in patients with and without COPD.

MATERIALS AND METHODS

Study design and patients: This was a prospective observational study of hospitalized patients with CAP at the University of Louisville Hospital and the Louisville Veteran Administration Hospital from 01/04/2012 to 01/08/2012. Patients were grouped according to presence of COPD in the past medical history (CAP+COPD (+) vs. CAP+COPD (-)).

Neutrophil function-Exocytosis: Exocytosis of secretory vesicles (CD35) and specific granules (CD66b) was determined by measuring plasma membrane expression, using flow cytometry (mean channel fluorescence).

Neutrophil function-Phagocytosis and Respiratory Burst: To measure H2O2 production in phagocytes was analyzed for fluorescence intensity by flow cytometry. Systemic cytokines and chemokines: Luminescence technology, according to manufacturers’ instructions, was used to measuring systemic levels of IL-6, IL-8, IL-10, IP-10, IP-12p40, IL-1b, IL-1ra, TNF-α and IFN-γ. Statistical Analysis: The Mann-Whitney U test was used to compare cytokine and chemokine levels between the CAP-COPD (+) and CAP+COPD (-) groups. Systemic cytokines and chemokines:

RESULTS

A total of 40 patients with CAP were enrolled in the study. The patients’ characteristics for the CAP and no COP patients are depicted in Table1. Figure 1 depicts: (A) Basal or formyl-methionyl-leucyl-phenylalanine (fMLP)-stimulated exocytosis of specific vesicles (CD35 plasma membrane expression) from healthy donors, or CAP patients at day of enrollment, and (B) Basal, or fMLP-stimulated exocytosis of specific granules from healthy donors, or CAP patients at day of enrollment. Figure 2 depicts: (2A) Phagocytosis of S. aureus and (2B) Respiratory burst activity.

CONCLUSIONS

Neutrophil functional responses such as secretory vesicles and specific granule exocytosis, phagocytosis, and phagocytosis-stimulated respiratory burst induced by Staph-aurae in the not affected patient by the presence of COPD.

Systemic levels of cytokines and chemokine: IL-6, IL-8, IL-17, IL-10, IL-12p40, IL-1β, IL-1ra, TNF-α and IFN-γ was not different between CAP+COPD (+) and CAP+COPD (-) on admission day. Except for IL-10 which was higher in CAP+COPD (+) which may be explained due to steroids use in those patients.

The innate pulmonary response during an episode of CAP measured by cytokine production and neutrophil function is not different in patients with or without COPD.

Our data support the clinical concept that patients with COPD are not at risk for poor outcomes during an episode of Alveolar infection. The chronic inflammatory response in the airways of patients with COPD does not interfere with an appropriate acute inflammatory response during an episode of alveolar infection.

REFERENCES