Effect of Omega-3 Polyunsaturated Fatty Acids on Inflammatory Biomarkers in Chronic Obstructive Pulmonary Disease

Dr. Amal Al-Haidose
Supervised by: Dr. Jeremy Allen
Biomedical Science Department, College of Health Sciences, Qatar University, Doha, Qatar

ABSTRACT
Chronic obstructive pulmonary disease (COPD) is a chronic progressive inflammatory disease characterized by airflow limitation. Several pro-inflammatory markers are thought to be involved in the pathogenesis of COPD. Cigarette smoking is a major risk factor for COPD and may be a modifiable risk factor for its progression & management. Dietary supplementation with omega-3 polyunsaturated fatty acids (Ω-3 PUFAs) may be effective therapeutically in patient COPD. Aim: To determine the plasma basal level of inflammatory biomarkers in the study population, to determine the inflammatory biomarkers release from Peripheral blood mononuclear cells (PBMCs), and to investigate the effect of omega-3 PUFAs on inflammatory biomarkers released from PBMCs. Methods: Blood samples were collected from 43 subjects; patients with COPD, 15 healthy smokers (HS), and 12 healthy groups (HGS). Selected biomarkers level was measured in Plasma and PBMCs by ELISA. Individual lipid profile analysis was carried out on RBCs fraction. Result: Plasma high levels of CRP and Fibrinogen and low level of CC-16 were observed in COPD patients when compared with healthy controls. The baseline release of IL6, ILB, TNFα, and CC16 from PBMCs was significantly differing in COPD and HS groups compared to HGS group. Omega-3 PUFAs (EPA and DHA) reduce IL-6, IL-8 and TNFα release from PBMCs. The fatty acid composition of the erythrocyte membranes in patients group was unmodified. Conclusion: This study showed that high level of several biomarkers that were detected systemically in COPD group may associate with the disease systemic inflammation. EPA and DHA possess the ability to reduce the cytokines production from COPD inflammatory immune cells. Additionally, no correlation was observed between fatty acid profile analysis and COPD.

INTRODUCTION
COPD is a multiplicative chronic lung disease that decreases quality of life due to shortness of breath and chronic cough. Alterations in the lungs including, destruction of the lung parenchyma and alveoli, inflammation of the central airways with chronic bronchitis, and emphysema of the small airways with chronic bronchitis (Tuder and Petracchi, 2012). This results in dyspnea, progressive airflow obstruction that is not fully reversible, productive cough, fatigue, and exacerbations (Fulton et al., 2013). Lung inflammation can pass through the systemic circulation causing systemic inflammations and comorbidities, including cardiovascular disease, lung cancer, skeletal muscle dysfunction, diabetes, osteoporosis, and cachexia. (Lee et al., 2018).

Several biomarkers involved in the pathophysiology and inflammatory process of COPD have been identified and measured, but little is known about their relationship to COPD development, progression and severity (Korai et al., 2016). There is a need for biomarkers for better evaluation of patients with COPD. This study aims to test the hypothesis that levels of inflammatory biomarkers are increased in circulation and from inflammatory cells in patients with COPD comparing to healthy subjects. Identification of plasma, pulmonary, and inflammatory immune cell biomarkers may facilitate improved diagnosis and prognosis in COPD.

RESULTS

- Linear regression analysis showed a significant correlation between FVC% and age (P=0.0009) and BMI (P=0.024) of the entire study subjects (P=0.05), and a significant correlation between FVC/FVC ratio and age (P=0.001), BMI (P=0.009) as well as weight of entire study subjects (P=0.022) (Figure 1).
- The mean value of plasma level of CRP was significantly higher in patients with COPD (15.48±28 mg/L) when compared to those of healthy nonsmoking individuals (2.27±2.92 mg/L) (P=0.007). Mean value of fibrinogen was significantly higher in COPD patients (1091±181 mg/dl) when compared with healthy smokers (136±66 mg/dl) (P=0.001). The mean value of CC16 was significantly lower in plasma of COPD group (2.75±1.19 mg/L) compared to healthy nonsmoking group (5.77±4.66 mg/L) (P=0.014) (figures 2).
- PBMCs obtained from COPD patients, released greater amounts of IL-6 (4±0.46 ng/ml), IL-8 (16.3±0.22 ng/ml), and TNFα (219±22 pg/ml), compared to those obtained from healthy nonsmokers (P=0.001) (Figures 3).
- There were no significant differences in fatty acids measurements (ARA/ EPA, omega-3 PUFA/Total PUFA and Omega 3-index) between the COPD group, healthy smokers and healthy nonsmokers groups (Figure 4).

CONCLUSION
Subject parameters; age, weight and BMI, have an impact on subject respiratory function when investigating the whole study individuals. High level of plasma CRP, fibrinogen, and low level CC16 were associated with COPD, which suggests that CRP, fibrinogen, and CC16 might be a useful biomarker panel related to the presence of COPD. Circulating PBMCs isolated from COPD patients show a profile of pro-inflammatory biomarkers distinct from control PBMCs. The data also confirmed that EPA and DHA individually exerted potential immunomodulatory effects characterized by significant reductions in PHA-induced cytokines release. Additionally, RBC membrane Omega-3 PUFA does not seem to have a major protective effect on lung function or disease symptoms. For better understanding of the COPD variability between patients, different parameters should be evaluated during patient diagnosis at routine clinical practices, including lung plethysmography, gas transfer, arterial oxygen, and CT, Pulmonary and systemic markers, and multiple spirometry. This will provides with accurate diagnosis and better disease management.

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REFERENCES