Biomarkers in Chronic Obstructive Pulmonary Diseases

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Editorial

Chronic obstructive pulmonary disease (COPD) is considered as a chronic inflammatory disease which is non-specific in nature involving the airway, lung parenchyma and pulmonary vessels which progressively leads to decrease in the airflow. Initiating factors for this inflammatory occurrence, which is not normal, are the toxic environmental conditions and the inflammation often remains even after eradication of the disturbing agent. This non-specific inflammation can activate a variety of inflammatory cells like neutrophils and macrophages and release of various inflammatory mediators, such as IL-8, IL-6, and TNF-α [1, 2]. These inflammatory mediators destroy the lung architecture and also promote the neutrophilic inflammatory response.

Many aspects have been considered for the fast drop in the lung function. Such as chronic bronchitis, existence of emphysema, present smoking, bronchodilator feasibility and recurring exacerbations are the few important ones [3, 4]. Recently, few ventures have shown to improve the lung function conditions other than smoking discontinuance. Spirometry results have shown that COPD people have a number of phenotypes with different changes in lung function, (e.g. sustainers, slow decliners, rapid decliners), on the basis of the preceding hazardous factors. However, it is difficult to state and understand the fact that how few patients survive lung disorders while others while others decline [3].

The ECLIPSE results have revealed variations in FEV1 in 2,163 patients with mild to critical COPD over the course of 3 years. Traditionally known biomarkers of the disease activity were analyzed, including fibrinogen, C-reactive protein, surfactant protein D, and interleukin 8. The decline in the rate of lung function was found associated with Clara Cell Secretory Protein [3]. Similarly, 4,724 patients were found to be suffering from mild to moderate COPD in the Lung Health Study, where less amount of serum levels of Clara Cell Secretory Protein were related to a rapid decline [4]. Recent studies have aimed at discovering a biologic mechanism responsible for the changes in the lung function deterioration.

Adiponectin (APN) is one of the cytokines mainly secreted by adipose tissue. Adiponectin, also known as GBP28 or AdipoQ, is a 244-residue protein produced mainly by white adipose tissue (WAT). APN is structurally similar to that of collagens VIII and X and complement factor C1q [5, 6].

APN circulates in different molecular forms in the blood. It has been reported by Miller et al., that by screening bronchoalveolar lavage (BAL) fluids from chronic obstructive pulmonary disease-Emphysema (COPD-E) and control subjects the epithelial cells can also secrete APN. Immuno-histochemistry of lung sections in COPD-E patients' demonstrated markable levels of adiponectin and adiponectin receptor 1 (AdipoR1) but not AdipoR2 in the epithelial cells. At present, the mechanism of APN participation in the inflammation of COPD remains unknown. To find out its role in COPD inflammation, Miller et al. measured the concentration of APN in the serum and induced sputum in patients and explored its relationship with the percentage of neutrophils in the airway, IL-8, IL-6 and TNF-α. These studies encourage new insights into the expression of lung epithelial cells with adiponectin and functional AdipoR1 is, implying a significant autocrine and/or paracrine pathway for adiponectin to stimulate. Finally, they explained that adiponectin showed high expression in the lungs of human subjects with the COPD-E. Comparatively, people without COPD, when exposed to tobacco smoke shows down-regulation in adiponectin expression. The study summarized that expression of adiponectin by airway epithelium may regulate the inflammatory reaction in COPD by autocrine or paracrine pathways [7].

The relativity between circulating adiponectin and COPD has been reported by many clinical studies. Tomodo et al. [8], reported that the serum adiponectin levels surpassed in patients with COPD as compared to the controlled ones. Moreover the results were correlated with decrease in weight and systemic

swelling as determined by circulating TNF-a levels. Except for the residual volume, functioning of the lung has nothing to do with the serum adiponectin levels.

Study by Summer et al. [9], says mice deficient in adiponectin were more susceptible to developing emphysema, which implied that adiponectin might be involved in tissue repair rather than disease development.

A recent study by Waschki et al. [10], reported that the cause of mortality in patients with COPD is serum adiponectin. This study surveyed more than 200 patients and could not figure the specific disease related causes of mortality. These findings indicate that adiponectin serum concludes CVD and CHD desolation and mortality, but cannot be considered as the only reason for the mortality in COPD.

It is undetermined that if adiponectin is by chance responsible for the pathogenesis of CHD and CVD or it is only a biomarker. Earlier studies reported an unusual aspect of adiponectin considering its anti-atherogenic and anti-inflammatory properties. The interrelation between adiponectin serum and escalation in the hazardous respiratory conditions is not clear.

The rising risk of mortality can be one possible reason. It was also found that declined risk of CVD morbidity and mortality in patients with increased APN serum expression may suffer from high risk of mortality by the rapid occurrences of respiratory deterioration. Another possible reason is that the circulating adiponectin may perform as a marker of substandard systemic inflammatory occurrence in COPD and hence can be termed as a secondary marker for COPD. Considering this invariable assumption, adiponectin serum concentrations are increased during exacerbations compared to term of clinical constancy. A third possible reason is that adiponectin may have straight effects on disease evolution. For example, adiponectin is responsible for the increase in the consumption of fatty acid and glucose by peripheral tissues and advances energy dissipation, which in turn promotes to weight loss. Weight loss is hazardous factor for COPD evolution and respiratory mortality, although it is protective against cardiovascular mortality.

A hospital based comparative study in COPD patients was carried out by authors. The main purpose of the study was to investigate the relationship between the severity of systemic inflammation, pulmonary functions and cachectic state in patients with COPD. The study was designated as a case control study. Fifty one COPD patients and 30 normal healthy volunteers were studied as controls.

The main results of our study were as follows:

a. The highest APN levels were detected in patients of severe & very severe COPD who had the lowest FEV1.

b. APN negatively correlated with BMI and FEV1.

c. APN negatively correlated with FVC post bronchodilator BD% predicted & FEV1/FVC post BD% predicted.

We found significant increase in APN levels in varying degree of severity of COPD patients as previous studies by Uzum et al. [11], and Chan et al. [12], have shown. But in contrast to our findings, Tomoda et al. [8] and Kirdar et al. [13], observed no relationship between lung function and plasma APN.

COPD being a progressive disorder with high morbidity and mortality needs a meticulous and scientific approach to its management. Evaluation of rate of progression and severity is mandatory in order to plan a rational treatment. In this regard biomarkers will be of immense value. Leptin and APN have shown that COPD has a systemic implication [14]. Estimation of multiple biomarkers in future may help in more rationalized approach to management of COPD by enabling us to know the severity, structural and functional deterioration and response to treatment.

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