# Abstract


***Background:***

Chronic obstructive pulmonary disease (COPD), a condition characterized by airway limitation, inflammation and long-term lung function decline, is a leading cause of mortality in the world. Lung function decline has been shown to predict both cardiovascular mortality and total mortality. In addition, a higher rate of decline in lung function has been associated with increased risks of both mortality and hospitalizations related to COPD. Thus, COPD should be regarded as a pulmonary disease, but these significant comorbidities must be taken into account in a comprehensive diagnostic assessment of severity and in determining appropriate treatment. The diagnosis of COPD is made based on the patient's symptoms, including cough, sputum production and dyspnea, and a history of exposure to risk factors such as tobacco smoke and occupational exposures. In COPD, airway pro-inflammatory cytokine levels including IL-8 and TNF-alpha have been demonstrated to be associated with increased airway obstruction and exaggerated airway inflammatory response. Oxidative stress is increased in patients with COPD, particularly during exacerbations, and it contributes to its pathophysiology. Many epidemiologic studies showed that subjects with COPD have a cardiovascular risk three times higher than healthy population and the cardiovascular mortality accounts for about the 50% of the overall observed mortality. Moreover studies showed that the incidence of coronary artery disease is directly related to the progressive FEV1 worsening. Recently statins have emerged as a possible disease modifying agents in COPD. The rationale for this at least partly derives from the fact that the pathogenesis of COPD involves inflammatory processes, and

persistent systemic inflammation seems to be present even in patients with stable COPD who do not currently smoke. There have been several recent pharmacoepidemiologic studies that have demonstrated that statin and/or ACE inhibitor use were associated with improved outcomes for patients hospitalized with acute COPD exacerbations or for those with pre-existing COPD.

## *Objective:*

The aim of this study is to evaluate the effect of simvastatin, telmisartan or their combination on pulmonary functions (FEV1, FEF25-75%, PEF and FEV3) and cardiovascular risk factors (hs-CRP, VCAM-1 and lipid profile) in COPD patients by affecting the inflammatory (hs-CRP) and immune processes (TNF-alpha) in addition to the oxidative stress (MDA). This work was carried out at Al – Basra General Hospital from December 2009 until June 2011 under the supervision of a specialist in internal medicine with a complete authorization from the ministry of health.

## *Subjects and methods:*

Eighty patients with mild to moderate COPD were successfully selected to participate in this study with age of 40-65years (mean = 58.8 ± 9.1). These patients were recruited into four groups where the first group included 20 patients on an inhaled β2- agonist (salbutamol 200-800 mcg/d) only (control), the second group included 20 patients on an inhaled β2-agonist plus 20mg/d simvastatin, the third group included 20 patients on an inhaled β2- agonist plus 40mg/d telmisartan and the fourth group included 20 patients on an inhaled β2- agonist plus combination of both simvastatin and telmisartan. Spirometric assessment of FEV1, FEF25-75%, PEF and FEV3 (by spirolab Ⅲ apparatus) was done for these patients at zero time and after 3 and 6 months of treatment with either simvastatin

20mg/d, telmisartan 40mg/d or combination of both. Twenty subjects who were apparently healthy selected as a normal group for the purpose of comparison. Mean age for these subjects was 59.09 ± 8.71. Fasting blood specimens were obtained to perform specific biochemical investigations also at zero time and after 3 and 6 months of drug treatment. Biochemical investigations included measuring serum levels of tumor necrosis factor-alpha (TNF – α), malonyldialdehyde (MDA), high sensitivity C- reactive protein (hs – CRP), vascular cell adhesion molecule-1 (VCAM1), lipid profile, creatine phosphokinase (CPK), creatinine, urea, serum glutamate oxaloacetate transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT).

## *Results:*

The results of the present work showed that patients with mild to moderate COPD had a lowered pulmonary function due to the presence of systemic inflammation and elevated immune markers in addition to the elevated oxidative stress, which may lead to increase risk for cardiovascular diseases. Treatment with simvastatin, telmisartan or their combination was associated with improved pulmonary outcomes by affecting the inflammatory and oxidative stress processes and this was illustrated by improvements in FEV1, FEF25-75%, PEF and FEV3 and reductions of TNF-α and MDA. Cardiovascular risks that have been elevated due to the disease progression were also modulated by the use of these drugs. This was confirmed by the reduction in hs-CRP, VCAM-1 and lipid profile. Liver function, renal function and skeletal muscle function have never been affected significantly during the study courses.

## *Conclusion:*

In conclusion, the anti-inflammatory, antioxidant and immunomodulatory effects of simvastatin and telmisartan were associated

with improved pulmonary function and decreased cardiovascular risk markers without affecting hepatic, renal and muscular functions, moreover, combination of both drugs was more effective than either drug alone which probably indicate a potentiation in the effect between statins and ARBs which require further studies.