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Lipid Profile Status in Mustard Lung Patients and Its Relation to Severity of Airflow Obstruction

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ABSTRACT

Introduction: Chronic obstructive pulmonary disease (COPD) secondary to sulfur mustard gas poisoning, known as mustard lung, is a major late pulmonary complications in chemical warfare patients. Serious comorbidities like dyslipidemia are frequently encountered in COPD. The aim of this study was to measure the serum lipid profile and evaluate the relation of lipid parameters with the severity of airway obstruction in mustard lung patients.

Materials and Methods: Thirty-six non-smoker mustard lung patients with no history of cardiovascular disease, diabetes mellitus, and dyslipidemia were entered into this cross-sectional study. Control group consisted of 36 healthy non-smoker men were considered in this study. Serum lipid profile was performed in the patients and the controls. Spirometry was done in mustard lung patients.

Results: The mean age of the patients was 47±6.80 SD years. The mean duration of COPD was 18.50±7.75 SD years. There were statistically significant differences in mean serum triglycerides and total cholesterol levels between patients and controls (P=0.04 and P=0.03, respectively).The mean levels of lipid parameters were not statistically significant different among the 4 stages of COPD severity (P>0.05).

Conclusion: The current study revealed that the serum levels of triglycerides and cholesterol are elevated in mustard lung patients compared with the healthy controls. Since lipid profile abnormalities are considered as a major risk factor for cardiovascular disease, especial attention to this matter is recommended in mustard lung patients.

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Introduction

Sulfur mustard (SM) as a toxic alkylating gas and chemical warfare agent, can cause serious late pulmonary complications including: asthma, bronchiectasis, bronchiolitis oblitrans, pulmon-

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ary fibrosis, and chronic obstructive pulmonary disease (COPD) (1-3). COPD due to SM poisoning, known as "Mustard Lung", is one of the important late pulmonary concerns in chemical warfare patients (4, 5). COPD is characterized by irreversible airflow obstruction in response of the lungs to inhalatory noxious gases (6). COPD is considered to be the third leading cause of death by A2020 (7). It is well accepted that COPD is not confined to the lungs and is now considered as a systemic inflammatory condition (8) and inflammatory biomarkers like highly sensitive C-reactive protein (hs-CRP), interleukins (IL), etc may be related to the pathogenesis of COPD (9). The role of systemic inflammation in mustard lung is still a matter of debate. Previous studies in mustard lung patients have shown that inflammatory biomarkers like hs-CRP and IL-6, are elevated in patients and have related to severity of airway disease (1, 9). In relation to systemic inflammation, several comorbidities like hypertension, diabetes mellitus, dyslipidemia, and cardiovascular disease are associated with COPD (10). Cardiovascular disease is the most common cause of mortality in COPD patients and dyslipidemia is considered a major risk factor for cardiovascular disease (10). The exact prevalence of lipid profile abnormalities in COPD are not determined (11). Previous studies in COPD patients have shown that the prevalence of dyslipidemia is significantly higher in COPD patients comparing to the healthy controls (7). The possible mechanisms of lipid profile abnormalities in COPD are: systemic inflammation, smoking, and physical inactivity (12, 13). The frequency of lipid profile abnormalities in mustard lung patients is not defined yet. Recently a study in chemical warfare patients has shown that serum total cholesterol (TC) and triglycerides (TG) are increased comparing to the healthy controls (14). Since smoking per se can cause major changes in serum lipid profile and as smoking is a major risk factor in COPD, the evaluation of serum lipid abnormalities in non-smoker COPD patients seems to be necessary.

This study was performed to evaluate the serum lipid profile in non-smoker mustard lung patients and to compare the results with the normal healthy controls. Also we aimed to determine the possible correlation of serum lipid abnormalities with severity of airway obstruction.

Materials and Methods

Thirty-six mustard lung patients who had documented SM poisoning history entered into this cross-sectional study from April 2012 to September 2012, Ghaem Hospital, Mashhad, Iran. All the participants were male. According to the definition of American Thoracic Society (ATS), patients who had irreversible airway obstruction [(forced expiratory volume in one second (FEV1) to forced vital capacity (FVC) less than 70% after 400 µgr Salbutamol inhalation] were considered to have COPD (15).One respiratory physician visited all patients. The patients were excluded if they had Asthma, bronchiectasis, tuberculosis, acute pulmonary infection, cardiovascular disorder and other systemic illnesses (e.g. diabetes mellitus, dyslipidemia); if they were taking systemic steroid, lipid lowering agents; if they had COPD exacerbation or hospitalization during the last 2 months; and if they were current or ex-smoker. Body mass index (BMI) was calculated as weight (kg) to height (m^2). By standard spirometeric techniques FEV1, FVC and FEV1/FVC were measured (multifunctional spirometer HI-801; chest MI Inc,Tokyo,japan). The severity of COPD was evaluated according based on GOLD (global initiative for chronic obstructive lung disease) guidelines (6) as following:

Stage 1 (mild): FEV1/FVC<70%, FEV1≥ 80%
Stage 2 (moderate): FEV1/FVC<70%, 50%≤FEV1 <80%
Stage 3 (severe):EV1/FVC<70%,30%≤FEV1<50%
Stage 4(very severe):FEV1/FVC<70%,FEV1<30%

Thirty-six healthy non-smoker men were considered as control group and the age and BMI of the controls were matched with patients. The control group was selected from Mashhad metabolic syndrome cohort study (16).

After 14 hours fasting, 5 milliliter blood samples were obtained from antecubital vein both in the patients and the controls. After centrifuge of blood samples, the serum samples were isolated and stored at -70 ^{oc} prior to analysis. Serum TG, TC, high density lipoprotein (HDL) were determined by routine enzymatic methods (Pars Azmoon ,Tehran,Iran).

This study was approved by the Ethics Committee of the Mashhad University of Medical Sciences (MUMS), code number: 89456. All patients provided informed consent.

Statistical analysis

The data were analyzed using statistical package for social sciences (SPSS, version 11.5, Chicago, IL, USA). For summarizing the clinical and biochemical findings of the groups, descryptive statistics were used. The continuous data were presented as percentages and means ± SDs. The normality of continuous variables was checked using the one sample Kolmogorov-Smirnov test. For continuous and categorical variables, independent student's t tests and chi-square tests were used to evaluate the statistical significance of any difference or relationship

Table 1. The clinical and biochemical findings in mustard lung patients and controls.

Data	Patients*	Controls*	P value**
Age (years)	47±6.80	46.50±6.10	0.53
BMI	26.50±4.55	25.80±4.35	0.80
TG(mg/dl)	181±41.80	130±64.50	0.04
TC(mg/dl)	210..40±34.55	160.23±45.60	0.03
LDL(mg/dl)	112.17±30.26	98.18±43.5	0.1
HDL(mg/dl)	46.23±4.95	42.34±5.5	0.5

* Data are presented as mean±SD.
**P* value<0.05 was considered significant.
BMI: Body Mass Index, HDL: High Density Lipoprotein, LDL: Low Density Lipoprotein, TC: Total Cholestrol, TG: Triglicerides.

between parameters, respectively. Pearson and Spearman correlation coefficients were calculated. A p Values less than 0.05 was considered significant.

Results

The mean age of mustard lung patients was 47±6.80 SD years. The frequency of different GOLD stages is shown in Figure 1. The mean duration of COPD was 18.50±7.75 SD years. The mean FEV1 was 2.78±0.85 SD liter. Twenty-six patients (72%) were received inhaled corticosteroids (ICS) and 5 patients were on home oxygen therapy.

The clinical and biochemical findings in the patients and the controls are shown in Table 1. As it has shown in Table 1, there were statistically significant differences in mean TC and TG between the patients and the controls.

The correlation of FEV1 with TG, TC, LDL, and HDL are shown in Table 2 that were not significant. Additionally, There were no statistically significant differences in mean serum levels lipid profile among the GOLD stages [TG (*P*=0.20), TC (*P*=0.07), HDL (*P*=0.10), and LDL (*P*=0.15)].

We calculate the TC/HDL in patients and 24 patients (66%) had a ratio >4. There was no statistically significant correlation between TC/HDL and FEV1 (r=0.15, *P*=0.41).

Table 2. The correlation of FEV1 with lipid profile parameters in mustard lung patients.

Parameter	P value*	Correlation Coefficient
TG(mg/dl)	0.65	0.20
TC(mg/dl)	0.42	0.25
LDL(mg/dl)	0.90	0.20
HDL(mg/dl)	0.50	0.10

* *P*<0.05 was considered significant.
HDL: High Density Lipoprotein, LDL: Low Density Lipoprotein, TC: Total Cholestrol, TG: Triglycerides.

Discussion

Since comorbidities have an important role in COPD morbidity and mortality, we evaluated the serum lipid profile in chemical warfare patients with COPD in this study. We found statistically significant differences in mean serum levels of TG and TC between the patients and the controls. The serum levels of TG, TC, LDL, and HDL did not have correlations with the severity of airflow limitation.

As we mentioned earlier, now COPD is considered a systemic inflammatory condition (8). The possible mechanisms of systemic inflammation are: genetic and constitutional factors, spillage of respiratory inflammatory mediators into systemic circulation, systemic inflammation involving the lungs, and smoking (17-20). In relation to systemic inflammatory condition in COPD, important comorbidities are highlighted in process of the disease. One of the main comorbidites in COPD is cardiovascular disease. Previous studies have shown that more than 50% of COPD patients have cardiovascular disease (10). COPD, independent of other major cardiovascular risk factors are associated with increased cardiovascular disease (21). The exact mechanism of increased cardiovascular risk in COPD is not defined yet (22), systemic inflammation and increased relevant biomarkers like hs-CRP may be concerned. The identified risk factors for accelerating atherosclerosis in cardiovascular system are: hypertension, diabetes mellitus,

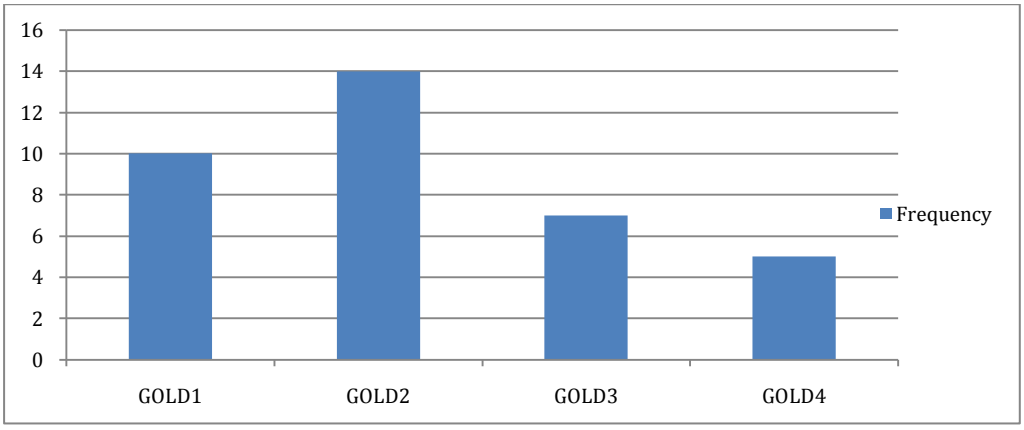

Figure 1. The frequency of different GOLD stages in patients.
GOLD: Global initiative for Obstructive Lung Disease.

hyperlipidemia especially high LDL and low HDL, and smoking (22). One of the most important risk factors in cardiovascular disease is dyslipidemia (10). The prevalence of lipid profile abnormalities in COPD are different in studies and a range of 9-50% have been reported (23-25). Studies concerning the prevalence of cardiovascular disease in chemical warfare patients have shown that coronary atherosclerotic lesion and coronary ectasia are frequent in patients comparing normal population (26, 27). Additionally, Attaran and colleagues show that the serum level of hs-CRP, as a major risk factor for ischemic heart disease, was increased in mustard lung patients comparing to healthy controls (9).

We found a statistically significant difference in mean serum levels of TG and TC between the patients and the controls. This finding was compatible with the results of Keramati and colleagues in chemical warfare patients who reported the same (14). Also Begun and colleagues showed that all lipid parameters including TG, TC, LDL, and HDL are elevated in COPD patients (22). Although there are studies that have shown the serum of lipid parameters are not different from healthy controls (10).

In the present study, the mean levels of lipid parameters were not different in different stages of COPD according to GOLD classification. The finding was compatible with the results of Niranjan and colleagues (12). Additionally we did not find any correlation between FEV1 and lipid parameters in mustard lung patients.

Our study has several limitations: First is our small sample size especially regarding to the distribution of patients in different severity stages. Second is about measurement of other lipid-related parameters like: Apo lipoproteins.

Conclusion

Since the presence of significant comorbidities in COPD, in this study we evaluated the serum levels of lipid parameters in mustard lung patients. The serum levels of triglycerides and total cholesterol were significantly elevated comparing the healthy controls. The serum lipid profile did not correlate with the severity of COPD.

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Conflict of Interest

The authors declare no conflict of interest.

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