NJPPP National Journal of Physiology, Pharmacy & Pharmacology

DOI: 10.5455/njppp.2015.5.230920141
http://www.njppp.com/

RESEARCH ARTICLE

A STUDY OF OXIDATIVE STRESS, ANTIOXIDANT STATUS, AND TNF-α LEVEL IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Arun K Singh, Lalit P Meena, Arun Saravanan, Ravi Tandon

Department of Medicine, Institute of Medical Sciences, Banaras Hindu University, Varanasi, UP, India

Correspondence
Lalit P Meena
(drlalitmeena@gmail.com)

Received
18.08.2014
Accepted
20.09.2014

Key Words
Chronic Obstructive Pulmonary Disease (COPD); Oxidative Stress; Malondialdehyde (MDA); Tumor Necrosis Factor-α (TNF-α)

Background: Nearly all smokers show some evidence of lung and systemic cellular and/or humoral inflammation, only a few will experience an amplified response and develop chronic obstructive pulmonary disease (COPD). Several studies have shown systemic inflammation in COPD patients with increased neutrophil, macrophage and T lymphocyte numbers, and high concentrations of inflammatory mediators in peripheral blood (C-reactive protein, interleukin (IL)-6, IL-8, and tumor necrosis factor-α (TNF-α)).
Aims and Objective: To study oxidative stress, antioxidant status, and TNF-α levels in patients with COPD.
Materials and Methods: Forty-four COPD patients along with an equal number of age- and sex-matched controls were included in study. The levels of malondialdehyde (MDA; by thiobarbituric acid assay), assay of TNF-α (by TNF-α), and total antioxidant were measured.
Results: Malondialdehyde level was found to be significantly higher in all cases, and it was statistically significant in COPD patients with Global Initiative on Obstructive Lung Disease (GOLD) classification grades 2 and 3. Total antioxidant level was significantly lower in all the patients with COPD and was statistically significant in GOLD grades 2 and 3. Like MDA, TNF level was also significantly higher in all the cases with statistically significant increase in GOLD grades 2 and 3.
Conclusion: To better understand the role of these trace elements and oxidative stress in the pathogenesis and complications of COPD, it is recommended to carry out further clinical studies.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a type of obstructive lung disease. It is not fully understood how tobacco smoke and other inhaled particles damage the lungs to cause COPD. The most important process responsible for lung damage is long-term smoking as it causes airway inflammation characterized by neutrophil, macrophage and activated T lymphocyte infiltration, and by increased cytokine concentrations such as tumor necrosis factor-α (TNF-α), interleukins (IL-6), and IL-8.[1] Although almost all smokers show some evidence of lung and systemic cellular and/or humoral inflammation, only a few experience an amplified response and develop COPD.[2] Several studies have shown systemic inflammation in COPD patients with increased neutrophil, macrophage and T-lymphocyte numbers, and high concentrations of inflammatory mediators in peripheral blood (C-reactive protein (CRP), IL-6, IL-8 and TNF-α).[3] TNF-α is a powerful proinflammatory cytokine primarily produced by activated macrophages. Little is known about the mechanism of increased TNF-α concentration in the plasma of COPD patients, and its relationship with disease severity and active smoking has not been established.[4] We hypothesizd that active smoking may be associated with more severe systemic inflammation in COPD patients. To test our hypothesis, we analyzed concentrations of TNF-α, IL-6, IL-8, and CRP in the peripheral blood of current smoker and ex-smoker with COPD, with a wide range of airway current smoker and nonsmoker controls. Malondialdehyde (MDA) is one of the stable end products of lipid peroxidation (LPO). The objective of this study was to evaluate oxidative stress, antioxidant status and TNF-α levels in patients with COPD.

MATERIALS AND METHODS

The present study was conducted in the Department of General Medicine, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India, during

June 2012 to June 2013. Forty-four COPD patients along with an equal number of age- and sex-matched controls were included in study. The inclusion criteria were COPD at any stage (mild, moderate, severe, and acute exacerbation) and exclusion criteria were presence of co-morbid conditions such infectious disease, septicemia, Sickle cell disease, hypertension, diabetes, Alzheimer's disease, and Parkinson's disease. COPD patients taking drugs, such as multivitamins, antioxidants, lycopene, β-carotene, astaxanthin, selenium, green tea, that can have antioxidative effect were also excluded. Detailed history and clinical examination of each patient was carried out. All patients underwent routine investigations. About 10 ml blood sample was collected from study subjects, centrifuged, and stored at −20 °C. These samples were then subjected to estimate MDA level (by thiobarbituric acid assay; Philpot method), assay of TNF-α (by TNF-α (Human) ELISA KIT Protocol), and total antioxidant levels.

Statistical Analysis

The analysis was carried out using the SPSS 16 software. The various parameters studied during observation period were compared using χ^2-test for noncontinuous variables. For continuous variable Student's *t*-test and analysis of variance were used. For all analyses, *p*-value < 0.05 was considered as statistically significant.

RESULTS

This study consisted of 44 COPD patients and 44 controls. Age distribution pattern shows that maximum number of patients with COPD belong to age group above 60 years (47.7%), followed by patients aged 51–60 years (31.8%). The patients aged 40–50 years group had minimum (20.5%) prevalence of COPD. Of 44 patients, 32 (72.7%) were male and 12 (27.3%) female. Pack-year data show that most cases had pack-years of more than 20 years (21 cases, 47.72%). MDA level was significantly higher in all cases, and it was statistically significant in COPD patients in Global Initiative on Obstructive Lung Disease (GOLD) grades 2 and 3 (Tables 1 and 2). Total antioxidant level was significantly lower in all the patients with COPD and was statistically significant in patients in GOLD grades 2 and 3 (Tables 3 and 4). Like MDA, TNF level was also significantly higher in all the cases, with statistical significance in GOLD grades 2 and 3 (Tables 5 and 6).

Table 1: MDA level in COPD patients and controls

Group	MDA level in mmol/L (Mean ± SD)	*t*-Value	*p*-Value
Case	1.35 ± 0.52	12.823	<0.001
Control	0.33 ± 0.05		

Table 2: Comparison of Gold Grade with MDA level in cases and controls

GOLD grade	MDA level	F-value	*p*-Value
2	0.306 ± 0.043	18.640	<0.001
3	0.399 ± 0.039		
Controls	0.33 ± 0.05		

Table 3: Total antioxidant level between cases and controls

Group	Antioxidant level in mmol/L (Mean ± SD)	*t*-Value	*p*-Value
Case	0.041 ± 0.022	11.192	<0.001
Control	0.130 ± 0.047		

Table 4: Comparison of Gold Grade with total antioxidant level in cases and controls

GOLD grade	Total Antioxidant Level	F-value	*p*-Value
2	0.147 ± 0.045	8.606	<0.001
3	0.088 ± 0.012		
Controls	0.130 ± 0.047		

Table 5: TNF-α level between cases and controls

Group	TNF-α level in pg/L (Mean ± SD)	*t*-Value	*p*-Value
Case	0.886 ± 0.424	11.983	<0.001
Control	0.111 ± 0.059		

Table 6: Comparison of Gold Grade with TNF-α level in cases and controls

GOLD grade	TNF-α level	F-value	*p*-Value
2	0.711 ± 0.287	148.56	<0.001
3	1.303 ± 0.416		
Controls	0.111 ± 0.059		

The MDA levels in COPD patients with pack-year less than 10 years were lower and in patients with pack years 11–20 years and >20 years were statistically significant higher than the controls. The total antioxidant levels in COPD patients with pack-year less than 10 years and 11–20 years were higher and those in patients with pack-years >20 years the reduction was statistically significant when compared with the controls. The TNF-α levels in COPD patients with pack-year <10 years were lower and in patients with 11–20 years and >20 years, the increase was statistically significant higher than the controls.

DISCUSSION

This study shows that COPD was prevalent the most in cases aged more than 6o years and majority of them are men, which supports the findings of some previous studies.[5] Most cases had pack-years of more than 20. The exact threshold for the duration/intensity of cigarette smoking that will result in COPD varies from one individual to another.

In the absence of genetic/environmental/ occupational predisposition, smoking less than 10–15 pack-years of cigarettes is unlikely to result in COPD. However, the single best variable for predicting which adults will have airflow obstruction on the spirometry is a history of more than 40 pack-years of smoking.[6,7] MDA is a highly toxic product of the LPO of unsaturated fatty acids by free radicals. Because it is a stable product, this is the reason why it is used as the marker of oxidative damage of unsaturated fatty acids. In this study, the level of serum MDA was found to be significantly higher in cases (1.35 ± 0.52; $p < 0.001$) compared to healthy controls (0.33 ± 0.05). Similar result was found in a study by Bartoli et al.[8] In the present study, antioxidant level was found to be significantly lower in the COPD patients (0.041 ± 0.022; $p < 0.001$) compared to healthy controls (0.130 ± 0.047). These findings are similar to those reported in a study conducted by Pirabbasi et al.[9] The level of TNF-α was found to be significant higher in cases (0.886 ± 0.424; $p < 0.001$) compared to age- and sex-matched healthy controls (0.111 ± 0.059), which is similar to that reported in another study.[10] When comparative analysis was carried out according to GOLD grade, we found that in GOLD grade 2 the level of MDA was 0.306 ± 0.043 ($p < 0.001$) and that in GOLD grade 3 it was 0.399 ± 0.039 ($p < 0.001$). Similar result also found by Kluchová et al.[11] The mean value for antioxidant level was found to be 0.147 ± 0.045 ($p < 0.001$) in GOLD grade 2 whereas in GOLD grade 3 it was 0.088 ± 0.012 ($p < 0.001$), which shows antioxidant level significantly decreases as GOLD grade increases. The mean value of TNF-α level was 0.7111 ± 0.287 ($p < 0.001$) in GOLD grade 2 whereas that in GOLD grade 3 was 1.303 ± 0.416 ($p < 0.001$), which showed statistical significance and increase in TNF-α level with higher GOLD grade. Similar result was also reported by Von Haehling et al.[10] In the present study when comparative evaluation was performed between MDA level, total antioxidant, and TNF-α levels, the findings were similar to those reported in some previous studies.[12,13]

CONCLUSION

To better understand the role of these trace elements and oxidative stress in the pathogenesis and complications of COPD, we recommend further clinical studies with large number of patients and using more sophisticated techniques, to reach any conclusion so that antioxidants and mineral supplementations can be used for better management of COPD.

REFERENCES

1. Quint JK, Wedzicha JA. The neutrophil in chronic obstructive pulmonary disease. J Allergy Clin Immunol. 2007;119:1065-–71.
2. Løkke A, Lange P, Scharling H, Fabricius P, Vestbo J. Developing COPD: a 25 year follow up study of the general population. Thorax 2006;61:935-9.
3. Higashimoto Y, Yamagata Y, Taya S, Iwata T, Okada M, Ishiguchi T, et al. Systemic inflammation in chronic obstructive pulmonary disease and asthma: Similarities and differences. Respirology 2008,;13:128–33.
4. Broekhuizen R, Wouters EF, Creutzberg ECAS. Raised CRP levels mark metabolic and functional impairment in advanced COPD. Thorax 2006;61:17-–22.
5. Kojima S, Sakakibara H, Motani S, Hirose K, Mizuno F, Ochiai M, Hashimoto S, et al. Incidence of chronic obstructive pulmonary disease, and the relationship between age and smoking in a Japanese population. J Epidemiol 2007;17(2):54-60.
6. Qaseem A, Wilt TJ, Weinberger SE, Hanania NA, Criner G, van der Molen T, et al. Diagnosis and management of stable chronic obstructive pulmonary disease: a clinical practice guideline update from the American College of Physicians, American College of Chest Physicians, American Thoracic Society, and European Respiratory Society. Ann Intern Med 2011; 155:179.
7. Simel D, Rennie D. The rational clinical examination: Evidence-based clinical diagnosis. McGraw Hill. (Ed), New York: McGraw-Hill, 2008.
8. Bartoli ML, Novelli F, Costa F, Malagrinò L, Melosini L, Bacci E, et al. Malondialdehyde in exhaled breath condensate as a marker of oxidative stress in different pulmonary diseases. Mediators Inflamm 2011;2011:891752. doi: 10.1155/2011/891752
9. Pirabbasi E, Najafiyan M, Cheraghi M, Shahar S, Abdul Manaf Z, Rajab N, et al. What are the antioxidant status predictors' factors among male chronic obstructive pulmonary disease (COPD) patients? Glob J Health Sci 2012;5(1):70-8.
10. Von Haehling S, Hopkinson NS, Polkey MI, Niethammer M, Anker SD, Genth-Zotz S. Elevated TNF alpha production in whole blood in patients with severe COPD: the potential link to disease severity. Wien Klin Wochenschr 2009;121(9-10):303-8.
11. Kluchová Z, Petrásová D, Joppa P, Dorková Z, Tkácová R. The association between oxidative stress and obstructive lung impairment in patients with COPD. Physiol Res 2007;56(1): 51-6.
12. Arja C, Surapaneni KM, Raya P, Adimoolam C, Balisetty B, Kanala KR. Oxidative stress and antioxidant enzyme activity in South Indian male smokers with chronic obstructive pulmonary disease. Respirology 2013;18(7):1069-75.
13. Churg A, Dai J, Tai H, Xie C, Wright JL. Tumor necrosis factor-α is central to acute cigarette smoke–induced inflammation and connective tissue breakdown. Am J Respir Crit Care Med 2002;166(6):849-54.

Cite this article as: Singh AK, Meena LP, Saravanan A, Tandon R. A study of oxidative stress, antioxidant status, and TNF-α level in chronic obstructive pulmonary disease. Natl J Physiol Pharm Pharmacol 2015;5:105-107.
Source of Support: Nil
Conflict of interest: None declared