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Original Research Article

Assessment of Oxidative Stress Parameters in Individuals with Chronic Obstructive Pulmonary Disease

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Abstract

Background and Objectives: While a majority of individuals who engage in smoking exhibit discernible signs of both pulmonary and systemic cellular and/or humoral inflammation, only a limited subset undergoes an intensified response leading to the development of COPD. Numerous investigations have substantiated the existence of systemic inflammation in COPD-afflicted individuals. This study endeavours to examine the levels of oxidative stress, antioxidant status, and TNF-α in patients diagnosed with COPD.

Materials and Methods: A cohort of 89 COPD patients, matched by age and sex with an equivalent number of controls, was enrolled in the study. The assessment involved the quantification of malondialdehyde (MDA) levels, TNF-α assay, and total antioxidant levels.

Results: The analysis revealed a significantly elevated level of malondialdehyde in all cases, with statistical significance observed in COPD patients. Total antioxidant levels were notably diminished in all COPD patients, exhibiting statistical significance. Similar to MDA, TNF-α levels exhibited a significant increase across all cases.

Conclusion: The heightened malondialdehyde and TNF-α levels, coupled with diminished total antioxidant levels, underscore the imperative to delve deeper into the intricate interplay of trace elements and oxidative stress in the pathogenesis and complications of COPD. This necessitates the undertaking of further comprehensive clinical studies.

Keywords: Smoking, Oxidative Stress, Antioxidants, Chronic Obstructive Pulmonary Disease

Introduction

Chronic obstructive pulmonary disease (COPD) represents a form of obstructive lung disease, the precise mechanisms through which tobacco smoke and inhaled particles induce lung damage leading to COPD remain incompletely elucidated. Prolonged smoking, a pivotal factor, triggers airway inflammation marked by infiltration of neutrophils, macrophages, and activated T lymphocytes, alongside heightened concentrations of cytokines such as tumor necrosis factor-α (TNF-α), interleukins (IL-6), and IL-8. Despite the presence of evidence indicating lung and systemic cellular and/or humoral inflammation in nearly all smokers, only a minority undergo an amplified response resulting in COPD. Systemic inflammation in COPD patients is substantiated by studies revealing elevated numbers of neutrophils, macrophages, and T lymphocytes, accompanied by high concentrations of inflammatory mediators in peripheral blood, including C-reactive protein (CRP), IL-6, IL-8, and TNF-α [1-3].

TNF-α, a potent proinflammatory cytokine primarily originating from activated macrophages, poses an intriguing aspect. The mechanisms underlying the elevated concentration of TNF-α in the plasma of COPD patients remain unclear, and its correlation with disease severity and active smoking has yet to be firmly established [4,5]. Our

hypothesis posits that active smoking may be linked to more pronounced systemic inflammation in COPD patients. To assess this hypothesis, we conducted an analysis of TNF-α, IL-6, IL-8, and CRP concentrations in the peripheral blood of current smokers and ex-smokers with COPD, alongside a diverse range of airway controls, including current smokers and non-smokers. Additionally, we evaluated oxidative stress, antioxidant status, and TNF-α levels through the measurement of malondialdehyde (MDA), a stable end product of lipid peroxidation.

Materials and Methods

The study cohort comprised 89 individuals diagnosed with COPD, alongside an equivalent number of controls matched for age and sex. Inclusion criteria encompassed COPD at any stage (mild, moderate, severe, and acute exacerbation), while exclusion criteria comprised the presence of co-morbid conditions such as infectious disease, septicaemia, sickle cell disease, hypertension, diabetes, Alzheimer's disease, and Parkinson's disease. Additionally, COPD patients using drugs with potential antioxidative effects, such as multivitamins, antioxidants, lycopene, β-carotene, astaxanthin, selenium, and green tea, were excluded from the study.

A meticulous history and clinical examination were conducted for each participant, followed by routine investigations. Approximately 10 ml of blood was collected from the study subjects, centrifuged, and stored at -20°C. Subsequently, these samples underwent estimation of MDA levels, assay of TNF-α, and assessment of total antioxidant levels.

The data analysis employed the SPSS 20 software. The various parameters observed throughout the study period were compared using the chi square test for noncontinuous variables. Continuous variables were assessed using Student's t-test and analysis of variance. A p-value < 0.05 was considered statistically significant for all analyses.

Results

The study involved 89 COPD patients and 89 controls. The age distribution pattern revealed that the majority of COPD patients were above 60 years old (48%), followed by those aged 51–60 years (32%). The prevalence of COPD in the 40–50 years age group was the lowest at 20%. Among the 44 patients, 73.03% were male, and 26.97% were female. Analysis of pack-year data showed that a significant portion of cases (47.19%) had a history of more than 20 pack-years.

MDA levels were notably higher in all COPD cases, and this elevation was statistically significant in patients classified under Global Initiative on Obstructive Lung Disease (GOLD) grades 2 and 3. The total antioxidant level was significantly lower in all COPD patients, with statistical significance observed in those categorized under GOLD grades 2 and 3. Similarly, TNF levels were significantly elevated in all cases, with statistical significance observed in patients belonging to GOLD grades 2 and 3 (refer to Tables 1 and 2).

In COPD patients, the MDA levels demonstrated a pattern where patients with pack-years less than 10 had lower levels, while those with pack years 11–20 and greater than 20 exhibited statistically significant higher levels compared to controls. Similarly, total antioxidant levels in COPD patients with pack-years less than 10 and 11–20 were higher, but in patients with pack-years greater than 20, the reduction was statistically significant when compared with controls. Regarding TNF-α levels, COPD patients with pack-years less than 10 showed lower levels, while those with 11–20 years and greater than 20 years demonstrated statistically significant higher levels than the controls.

Table 1: MDA, Antioxidant and TNF-α levels in study population

Parameters	Cases (n=89)	Controls (n=89)	p Value
MDA mmol/L (Mean ± SD)	1.42 ± 0.48	0.29 ± 0.06	<0.05
Antioxidant level mmol/L (Mean ± SD)	0.038 ± 0.019	0.135 ± 0.051	<0.05
TNF-α pg/L (Mean ± SD)	0.902 ± 0.412	0.118 ± 0.062	<0.05

Table 2: Correlation of COPD severity with MDA, Antioxidant and TNF-α levels (Chi-Square test)

Parameters	GOLD grade 2	GOLD grade 3	Controls	p Value
MDA level	0.297 ± 0.047	0.408 ± 0.034	0.31 ± 0.06	<0.05
Antioxidant level	0.140 ± 0.040	0.095 ± 0.014	0.125 ± 0.042	<0.05
TNF-α level	0.690 ± 0.272	1.262 ± 0.404	0.120 ± 0.055	<0.05

Discussion

This study demonstrates a higher prevalence of COPD in individuals aged over 60, with a predominant occurrence among males, consistent with the observations from previous studies [5,6]. A significant proportion of cases had a smoking history of more than 20 pack-years. The threshold for cigarette smoking duration/intensity leading to COPD varies individually, and in the absence of genetic/environmental/occupational predisposition, it is improbable for COPD to manifest with smoking less than 10–15 pack-years. Notably, a history of more than 40 pack-years of smoking emerges as the most reliable predictor of airflow obstruction on spirometry [7,8].

MDA, a toxic by-product of lipid peroxidation (LPO) from unsaturated fatty acids by free radicals, serves as a stable marker for oxidative damage. In this study, serum MDA levels were significantly elevated in cases compared to healthy controls, corroborating findings by Bartoli et al. [9]. Furthermore, the antioxidant levels were markedly lower in COPD patients compared to healthy controls, aligning with results reported by Pirabbasi et al. [10].

The study also revealed a substantial increase in TNF-α levels in cases compared to age- and sex-matched healthy controls, mirroring findings in another investigation [11]. Comparative analysis based on the GOLD grades demonstrated a progressive increase in MDA levels from GOLD grade 2 to GOLD grade 3, consistent with Kluchová et al.'s observations [12]. Similarly, antioxidant levels declined significantly from GOLD grade 2 to GOLD grade 3, indicating a negative correlation with increasing GOLD grade. TNF-α levels also exhibited a statistically significant rise from GOLD grade 2 to GOLD grade 3, in line with previous reports [12].

Upon comparative evaluation of MDA level, total antioxidant, and TNF-α levels, the present study's findings parallel those reported in earlier investigations [13,14].

Conclusion

To gain a more comprehensive understanding of the role of trace elements and oxidative stress in the pathogenesis and complications of COPD, we advocate for additional clinical studies involving a larger cohort of patients. Employing more sophisticated techniques in these studies will enable a more nuanced exploration, facilitating the derivation of meaningful conclusions. This, in turn, could pave the way for the consideration of antioxidants and mineral supplementation as potential strategies for the enhanced management of COPD.

References

1. 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.
2. Quint JK, Wedzicha JA. The neutrophil in chronic obstructive pulmonary disease. J Allergy Clin Immunol. 2007;119:1065-71.
3. 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.
4. 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.
5. Broekhuizen R, Wouters EF, Creutzberg ECAS. Raised CRP levels mark metabolic and functional impairment in advanced COPD. Thorax. 2006;61:17-22.
6. 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.
7. 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.
8. Simel D, Rennie D. The rational clinical examination: Evidence-based clinical diagnosis. McGraw Hill. (Ed), New York: McGraw-Hill, 2008.
9. 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 various pulmonary conditions. Mediators Inflamm 2011;2011:891752.
10. Pirabbasi E, Najafiyan M, Cheraghi M, Shahar S, Abdul Manaf Z, Rajab N, et al. Factors predicting antioxidant status among male chronic obstructive pulmonary disease (COPD) patients. Glob J Health Sci 2012;5(1):70-8
11. 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.
12. 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.
13. 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.
14. Churg A, Dai J, Tai H, Xie C, Wright JL. Tumor necrosis factor-alpha is central to acute cigarette smoke–induced inflammation and connective tissue breakdown. Am J Respir Crit Care Med 2002;166(6):849-54.