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ORIGINAL ARTICLE

Role of oxidant–antioxidant imbalance in the pathogenesis of chronic obstructive pulmonary disease

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KEYWORDS

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Catalase;
Nitric oxide

Abstract *Background:* Chronic obstructive pulmonary disease (COPD) is a common respiratory condition involving the airways and characterized by airflow limitation. Antioxidants are substances that may protect cells from the damage caused by unstable molecules known as free radicals. Antioxidants interact with and stabilize free radicals and may prevent some of the damage free radicals might otherwise cause. Under physiological conditions a balance exists between the amount of reactive oxygen species (ROS) produced in normal cellular metabolism and the endogenous antioxidant defense. An imbalance between the antioxidant capacity and the production of reactive oxygen species leads to oxidative stress, which is associated with the pathogenesis of several human diseases. An oxidant/antioxidant imbalance has been proposed as having a key role in the pathogenesis of COPD. The lung is directly exposed to high levels of oxygen, and therefore has to have efficient antioxidant mechanisms.

Aim of the study: To examine the role of altered levels of oxidant–antioxidants in disease severity of COPD and correlate it with the degree of airflow obstruction in the Egyptian population.

Subjects and methods: Eighty subjects with COPD, 20 healthy smokers, and 20 healthy nonsmokers participated in this study. The investigation included determination of the lung function and the measurements of plasma superoxide dismutase activity (SOD), glutathione content (GSH) reduced form, glutathione peroxidase activity (GSH-Px), catalase activity (CAT), lipid peroxidase (LP), and nitric oxide (NO).

Results: The mean concentration of nitric oxide (NO) was significantly higher in the control subjects (smokers and nonsmokers) compared with the COPD group ($p = 0.001, 0.0001$) respectively.

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Also the mean concentration of nitric oxide (NO) was significantly higher in control nonsmoker group compared to control smoker group ($p = 0.002$). The mean concentration of lipid peroxidase (LP) was significantly higher in COPD patients compared with control subjects (smokers and nonsmokers), ($p = 0.0001, 0.0001$) respectively. The mean concentration of glutathione (GSH) was significantly higher in the control subjects (smokers and nonsmokers) compared with COPD patients ($p = 0.001, 0.001$) respectively. There is no significant difference in the concentration of glutathione-peroxidase (GSH-Px) in all study participants (COPD patients, control smokers, control nonsmokers). The mean concentration of catalase (CAT) was significantly higher in control nonsmokers, compared to COPD patients and control smokers ($p = 0.001, 0.018$) respectively. The mean concentration of superoxide dismutase (SOD) was significantly higher in the control subjects (smokers and nonsmokers) compared with COPD patients ($p = 0.012, 0.001$) respectively. Also the mean concentration of superoxide dismutase (SOD) was significantly higher in control nonsmoker group compared to control smoker group ($p = 0.001$).

Conclusion: These results support the hypothesis that an oxidant–antioxidant imbalance, associated with oxidative stress in COPD patients, plays an important role in the progression of disease severity, also these results revealed the presence of an oxidative presence in smokers and in subjects with COPD and that the imbalance may be important in the pathogenesis of this disease. The use of cigarette increased oxidative stress by causing plasma lipid peroxidation and imbalance in erythrocyte antioxidant. Nitric oxide (NO) metabolism was not increased in patients with chronic obstructive pulmonary disease compared to healthy subjects. It has been reported that GSH plays a major role in pulmonary antioxidant protection.

Introduction

Human ecology requires both oxygen and water with the generation from food of an immediate energy source, ATP, by oxidative phosphorylation. A continuing balance between oxidation and anti-oxidation is necessary for longer less-disabled lives, taking account of oxidative stresses and the critical roles of oxidants in defense against infection, tissue repair and signaling [1]. There is no animal life without oxygen consumption and its conversion to water with the production by leakage from mitochondrial electron transport of free radicals [2], in the course of oxidative phosphorylation and the production of ATP as the ultimate and immediate source of energy [3]. Free radicals may also be formed as nitrogen, carbonyl, chlorine, sulfur and other reactive species [4,5]. During oxidation electrons or hydrogen are transferred from one molecule to another, the latter serving as an antioxidant. Antioxidants, therefore, can stop the formation of free radicals and the chain reactions, which would otherwise result in cell damage or even death.

Oxidant–antioxidant and COPD

The airflow obstruction in COPD is associated with abnormal inflammatory response of the lungs to chronic inhalational exposure from smoke, dust particles and other air pollutants. As a result, the lungs lose their elasticity [6]. Apart from inflammatory reactions, the domination of proteinases over antiproteinases [7] and oxidative stress [8] are also important factors in the pathogenesis of COPD. It has been proven that the incidence of COPD is strictly correlated with the addiction to smoking tobacco [9,10]. It is considered that reactive oxygen species (ROS) is the major cause of cell and tissue damage associated with many chronic inflammatory lung diseases, including COPD [11,12]. Oxidative stress in cells and tissues is induced by the imbalance between the generation and removal of ROS. ROS are derived from inflammation inducing cells (neutrophils, macrophages), large numbers of which migrate to the lungs, also play an important role in the oxidant–antioxidant imbalance observed in the course of COPD [13]. However, the precise mechanism of the etiopathogenesis of COPD is not yet well defined. It is considered that the increased oxidant burden and oxidant–antioxidant imbalance might be the main cause of the disease (COPD) [14]. Increased oxidative burden is generated from airway leucocytes in the blood or in air spaces directly as a result of cigarette smoke and environmental oxidant pollutants, and indirectly by the release of increasing amounts of ROS. The ROS are scavenged by antioxidant compounds and enzymes [11]. Cigarette smoke is the main etiological factor in the pathogenesis of COPD, as it leads to oxidant overload in the lower airways. Cigarette smoke contains more than 1016–1017 oxidant molecules per puff and about 4700 chemicals, including peroxynitrite, superoxide radical and oxides of nitrogen [15]. The adverse contribution of cigarette smoke is considerable; however, the contribution of other risk factors is equally important, as all smokers do not develop COPD. Under normal conditions, the lungs and the blood are adequately protected by various extracellular and intracellular antioxidants against the deleterious effects of oxidants [16]. There is evidence to suggest an imbalance between oxidants and antioxidants in the lungs and the blood in smokers as well as in patients with COPD [17]. One of the results of increased ROS generation is increased lipid peroxidation. It involves free radical chain reactions leading to the decomposition of polyunsaturated fatty acids, constituting, for example, the components of cell membranes [18]. In this process, once a hydrogen atom is detached from a polyunsaturated fatty acid molecule, a reconfiguration of double bonds occurs and leads