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EVALUATION OF THE OXIDATIVE STRESS IN SILICOSIS PATIENTS

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ABSTRACT

Objective. Silica particles are potent inducers of cell proliferation, cell injury, and inflammation, and oxidant release from alveolar macrophages, thus providing a mechanistic framework for their increased fibrogenicity. The Alveolar macrophages are viewed as a pivotal cell type in fibrogenesis in both lung defense and elaboration of growth factors and oxidants**.** In this study, we aimed to investigate serum TAS (Total Antioxidant Status), TOS (Total Oxidant Status) and OSI (Oxidative Stress Index) parameters in the individuals working in ceramic factory and diagnosed as silicosis and discuss the possible effects of these parameters on the etiopathogenesis of the disease.

Methods. This study was performed on 33 male patients with silicosis (23-73 years) and 30 male healthy control (18-69 years) who were admitted to Ankara Occupational Diseases Hospital. Silicosis patients were diagnosed depending on their chest radiograms in accordance with the ILO 2000 guidelines. TAS, TOS levels were measured in blood samples and OSI was calculated according to formula (TOS/TAS).

Results. Serum TOS levels of the silicosis subjects were higher than those of the controls whereas serum TAS levels of silicosis subjects was lower than those of the controls. But the

differences between the parameters were not statistically significant. The serum OSI levels were significantly higher ($p<0.05$) in the silicosis subjects compared with the control group.

Conclusion. Our study showed elevated OSI in patients with silicosis. Increased oxidative stress is thougth to be related with the oxidative burst caused by alveolar macrophage activation.

Keywords. Silicosis**,** Total Antioxidant Status, Total Oxidant Status, Oxidative Stress

Conflict of interest: Authors do not have any conflict of interest

INTRODUCTION

Silicosis is a chronic inflammatory and fibrotic lung disease produced by the inhalation of one of free crystalline silicon dioxide or silica, most commonly quartz. Occupational exposure to respirable silica particles occurs in many industries. Silicosis is seen granite workers, among sandblasters, underground miners, foundry and quarry workers, and in the individuals working in ceramic factory (1, 2).

Silica particles are rapidly cleared from the lung, but inhaled very small silica particles, those less than 0.5 /μm, may be deposited small airways and alveoli (3). These particles are potent inducers of cell proliferation, cell injury, and inflammation, and oxidant release from alveolar macrophages (AMs), thus providing a mechanistic framework for their increased fibrogenicity (4, 5). Silica fibers are toxic to AMs, its increased redox potential and produce the damaging hydroxyl radical (6). In this way fibrotic events produces silicosis (7). Silica particles continues to different clinical and pathologic varieties of interstitial lung disease nodular silicosis, acute silicosis, progressive interstitial fibrosis (8). But many patients with simple silicosis are asymptomatic (9).

To our best knowledge, oxidative status of silicosis patients has not been investigated using serum total antioxidant status (TAS) and serum total oxidant status (TOS) measurement, oxidative stres index (OSI) calculation. In the this study we aimed to examine TAS, TOS and OSI levels to evaluate oxidative stress in the individuals working in ceramic factory and diagnosed as silicosis and discuss the possible effects of these parameters on the etiopathogenesis of the disease.

MATERIALS AND METHODS

Sample collection

This study was performed on 33 male patients with silicosis and 30 male healthy control who were admitted to Ankara Occupational Diseases Hospital. Silicosis patients were diagnosed depending on their chest radiograms in accordance with the ILO 2000 guidelines. Blood fasting specimens were collected in serum separator tube (BD Vacutainer®) and centrifuged at 1300 g for 10 minutes after comletion of clotting and stored at - 80 C0 until analysis.

Laboratory analysis

TAS method shows the antioxidative effect of the sample against the potent free radical reactions, which is initiated by the produced hydroxyl radical (10). TOS can be measured spectrophotometrically and colour intensity is related to the total amount of oxidant molecules present in the sample. The assay is calibrated with hydrogen peroxide (H2O2) (11). OSIcan be described as powerful parameter reflecting both oxidative and antioxidant status (12). Serum TAS (Total Antioxidant Status) levels were determined by using a colorimetric method. Analysis was carried out by using Rel Assay Diagnostics TAS (Total Antioxidant Status) kit (catalog no: RL0017) in Beckman Coulter AU680 autoanalyzer (Measuring range: 1.50 to 1.20 mmol / L).Serum TOS (Total Oxidant Status) levels were determinedby using spectrophotometric method. Analysis was carried out by using Rel Assay Diagnostics TOS (Total Oxidant Status) kit (catalog no: RL0024) in the Beckman Coulter AU680 autoanalyzer (measuring range: 4-6 micro mol / L).OSI (Oxidative Stress Index) was calculated by the TOS / TAS formula.

Statistical analysis

The findings of the study were analyzed with "The Statistical Package for Social Sciences for Windows ver.18" (SPSS Inc, Chicago, USA, 2009) software. The conformity of continuous variables to normal distribution was tested with Kolmogorov-Smirnov test. The descriptive statistics of continuous variables were expressed as mean ± SD or median (min-max). The presence of a statistically significant difference between the groups in terms of continuous variables was examined with the Student t test for parametric and Mann-Whitney U test for nonparametric variables. P value of < 0.05 was considered statistically significant for all tests.

RESULTS

33 male patients with silicosis (23-73 years) were included in this study. 30 male healthy control (18-69 years) were enrolled.

Serum TOS levels of the silicosis subjects were higher than those of the controls whereas serum TAS levels of silicosis subjects was lower than those of the controls. But the differences between the parameters were not statistically significant. Median of calculated OSI levels were 2,25 (0,76- 11,87) arbitrary unit in silicosis patients and 1,91 (0,81- 4,32) arbitrary unit in healthy group. The serum OSI levels were significantly higher (p=0.036) in the silicosis patients compared with the healthy group.

Table-1: Median values of serum TAS, TOS, OSI in silicosis patients and healthy control.

	Silicosis Patients n =33	**Healthy Control n =30**	**p**
TAS levels (mmol Trolox equivalent/L)	1,45 (1,17- 1,85)	1,52 (1,2- 2,12)	0,260
TOS levels (µmol H2O2 equivalent/L)	3,23 (1,38- 19,35)	2,88 (1,17- 6,87)	0,066
OSI (arbitrary unit)	2,25 (0,76- 11,87)	1,91 (0,81- 4,32)	0,036*

*Statistically significant (P<0.05)

Values are expressed as median (min-max)

DISCUSSION

Silicosis is one of the most important occupational diseases worldwide (13). Silica exposure has been associated with various disorders (tuberculosis, airway obstruction, and lung cancer) (14, 15). The US National Institute for Occupational Safety and Health and National Toxicology Program classified crystalline silica as a human carcinogen (16).

In our study, we observed that silicosis patients had oxidative/antioxidative balance towards oxidative status. We showed that OSI levels of silicosis patients were significantly different from the controls to indicate the presence of an increased oxidative stress.

Molecular, cellular and intracellular mechanisms are tried to explain silicosis. Small silica particles induces oxidant release from alveolar macrophages (AMs), cell injury and cell proliferation (17-19). The AMs are viewed as a main cell type in fibrogenesis in both lung defense (20). Silica can produce reactive oxygen species thus damaged particle surfaces by its effect on AMs (21). Oxidative stress is a state of imbalance in the reactive oxygen species (ROS) production and degradation. Small silica particles deposition causes formation of ROS that affects cell membranes with ascending lipid peroxidation and permeability while synchronously inactivates the anxioxidant enzymes (22). It is known that oxidative stress is one of the mechanisms in silicosis and ROS levels were examined in order to show oxidative stress status in several studies.

Also several studies have been done about lysosomal damage, activating the NALP3 inflammasome and triggering the inflammatory cascade by phagocytosis of silica particles in the lung causes.(23)

To sum up, this study showed elevated OSI in patients with silicosis. Increased oxidative stress is thought to be related with the oxidative burst caused by alveolar macrophage activation. OSI can be used to determine of the oxidative stress and provides information about the general oxidative status. As the measurement of TAS, TOS and OSI levels are easy and can be applied to the any automated analyzer.

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