INTRODUCTION

While considerable progress has been made in development of drugs for asthma, there have been few advances in the treatment of chronic obstructive pulmonary disease (COPD) (1). The inflammatory response in COPD is essentially steroid resistant and differs markedly from that of asthma so that alternative anti-inflammatory therapy is needed. New therapeutic approaches will arise out of better understanding of the disease process at cell and molecular level. Oxidative stress is implicated in the pathogenesis of several disease processes. An increasing amount of research has focused on the proposal that an oxidant/antioxidant imbalance occurs in smokers and in patients with COPD as part of the pathogenesis of the condition (2-4).

OXIDATIVE STRESS AND PROTEIN GLYCATION IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Abstract: Several studies have indicated the presence of increased oxidative stress as a critical feature in the pathogenesis of chronic obstructive pulmonary disease (COPD). Another biochemical complication leading to pathogenesis is protein glycation. The nexus between oxidative stress and protein glycation in various pathological conditions is being unraveled. Increased oxidative stress can lead to enhanced protein glycation by a process of auto-oxidative glycation. No information is available in the literature regarding protein glycation among COPD patients. Eleven non-diabetic COPD patients were included in the study and equal number of age and sex-matched healthy individuals were enrolled as controls. The whole-blood reduced glutathione was found to be less among the patients while lipid peroxides and fructosamine were elevated in comparison to control. The present study confirmed oxidative stress and enhanced protein glycation among the COPD patients. Antioxidant therapy may be considered as part of the treatment regimen for COPD patients.

Key words: COPD lipid peroxidation protein glycation

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and gene expression of pro-inflammatory mediators. Oxidative stress also has a role in enhancing the airway inflammation. Oxidative stress, measured as thiobarbituric acid reactive substances (TBARS) in plasma, has also been shown to correlate inversely with the percent predicted FEV₁ in a population study, indicating that lipid peroxidation is associated with airflow limitation in the general population (5). An association between dietary intake of antioxidant vitamins and lung function has been demonstrated in the general population (6). Another biochemical complication leading to pathogenesis is protein glycation (7). It is also implicated in the acceleration of normal aging process (8). The nexus between oxidative stress and protein glycation in various pathological conditions is being unraveled. Increased oxidative stress can lead to enhanced protein glycation by a process of auto-oxidative glycation (9). Although in-vitro experimental evidences are available in support of the hypothesis (10), not much information is available from in-vivo pathological situations. We have observed that in cases of non-diabetic renal failure, nephrotic syndrome, hyperthyroidism and rheumatoid arthritis, oxidative stress could enhance protein glycation (11–13). The present study was carried out to find out if COPD is associated with enhanced protein glycation and to elucidate the nexus between oxidative stress and protein glycation if any.

METHODS

Selection of cases and control: Eleven patients with COPD attending the Out Patients Department of Tuberculosis and Chest Disease, JIPMER hospital was included in the study. The diagnosis of COPD was based on clinical history, pulmonary function tests and X-ray. Eleven age and sex-matched control samples were collected from healthy individuals. Diabetic patients were excluded from the study. Ethics clearance for the study was obtained from Research Council, JIPMER, Pondicherry. The study was carried out with the blood samples collected for the routine biochemical investigations required by the clinicians for the patients. Five milliliters of fasting blood samples were collected in EDTA bottles for the study.

Assessment of biochemical parameters: Estimation of lipid peroxidase was carried out with thiobarbituric acid (14). Whole blood reduced glutathione (GSH) (Reference range: 2.02 ± 0.32 mg/g Hb) was estimated with Ellman's reagent and the results were expressed as mg per gram of hemoglobin (15). Plasma fructosamine (Reference range: 1.6–2.8 mmol/L) was estimated by p-indocyanine violet kinetic method using the Raichem kits (Hemagen diagnostics, San Diego, CA, USA) adapted to 550 express plus autoanalyzer (Ciba Corning Diagnostics, Oberlin, OH).

Statistical analysis: The data between control and test groups was compared using unpaired student\'s t test.

RESULTS

The whole blood reduced glutathione was found to be significantly reduced among the COPD patients in comparison to the age and sex-matched controls. The plasma lipid peroxides and plasma fructosamine were
has indicated that the process of protein glycation can be promoted by malondialdehyde (MDA), an end product of lipid peroxidation (17). However, the mechanism by which MDA enhances glycation of proteins has not been clearly defined. It is presumed that the aldehyde groups of MDA act as an anchor between sugar and protein moieties, thereby enhancing the formation of glycated proteins (17). In-vitro experiments have indicated that antioxidants such as vitamin C and glutathione play a possible role in preventing the process of protein glycation (18). An inhibiting effect of vitamin C on glycosylation of proteins has been reported (19). In our earlier studies in non-diabetic patients with undialyzed chronic renal failure, pediatric nephrotic syndrome, hyperthyroidism and rheumatoid arthritis, we found a nexus between oxidative stress and protein glycation (11–13). In the present study with non-diabetic COPD patients, we found a similar significantly enhanced protein glycation that could be attributed to the oxidative stress. A significant correlation between oxidative stress and protein glycation in the COPD patients could not be established and this might be due to the fact that they were under treatment. It will be interesting to know the effect of an early inclusion of antioxidant therapy in the treatment regimen on the level of protein glycation among the COPD patients.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control group</th>
<th>COPD group</th>
<th>'p' value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>54.72 (7.52)</td>
<td>56.54 (8.0)</td>
<td>0.58</td>
</tr>
<tr>
<td>Male / Female</td>
<td>9 / 2</td>
<td>10 / 1</td>
<td>-</td>
</tr>
<tr>
<td>Whole blood GSH (mg/g Hb)</td>
<td>1.79 (0.24)</td>
<td>1.37 (0.24)</td>
<td>0.00094</td>
</tr>
<tr>
<td>Plasma lipid peroxides (µM/l)</td>
<td>5.04 (0.64)</td>
<td>7.13 (1.99)</td>
<td>0.00363</td>
</tr>
<tr>
<td>Plasma fructosamine (mmol/l)</td>
<td>2.80 (0.552)</td>
<td>3.55 (0.716)</td>
<td>0.0109</td>
</tr>
</tbody>
</table>

A 'p'<0.05 was considered significant.

The results obtained indicate enhanced oxidative stress and protein glycation in the COPD patients. Since all the COPD subjects included in the present study were non-diabetic, enhanced protein glycation cannot be attributed to impaired glucose tolerance. Another cause for protein glycation is the prevailing oxidative stress. In vitro experimental evidences indicate that pro-oxidative forces can enhance protein glycation by autoxidative glycation and glycoxidation (16). In vitro study by Jain et al.

REFERENCES

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