Exhaled breath condensate levels of 8-isoprostane, growth related oncogene α and monocyte chemoattractant protein-1 in patients with chronic obstructive pulmonary disease

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Received 10 June 2005; accepted 5 August 2005

Summary Chronic obstructive pulmonary disease (COPD) patients have increased neutrophils and macrophages in their lungs, and inflammation of the airway is related to oxidative stress. This study assessed the levels of 8-isoprostane (an oxidative stress marker) and chemokines related to neutrophil and monocyte inflammation (growth-related oncogene α [GRO\textsubscript{α}] and monocyte chemoattractant protein-1 [MCP-1]) in the airway of ex-smoking COPD patients by exhaled breath condensate (EBC) collection.

Thirty-two (28 males) stable COPD patients (14 with FEV\textsubscript{1} > 50\% [Group 1], 18 with FEV\textsubscript{1} < 50\% predicted [Group 2]) and 18 non-smoking age and sex-matched controls were studied in this cross-sectional study. EBC was collected using the EcoScreen (Jaeger, Germany) during 10 min of tidal breathing with the nose clipped. Concentrations of 8-isoprostane, GRO\textsubscript{α} and MCP-1 were measured by enzyme immunoassays.

COPD patients had a higher concentration of 8-isoprostane than controls (COPD versus control, \(P<0.001\); Group 1 versus Group 2, \(P=0.045\)). 8-isoprostane increased across the groups from normal, Group 1 to Group 2 (\(r=0.64, P<0.001\)). The median intraquartile range (IQR) levels in pg/ml for GRO\textsubscript{α} were 45.3(44.5–46.5), 45.4(44.5–46.0), 46.0(45.6–47.3), whereas MCP-1 levels were 5.3(5.2–5.9), 6.2(5.4–6.9) and 5.7(5.5–6.4) in Group 1, Group 2 COPD and control subjects,

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Introduction

Increased oxidative stress\(^1\) and leukocyte infiltration in the airway\(^2\) are observed in patients with chronic obstructive pulmonary disease (COPD). Imbalance between oxidants and anti-oxidants in the airway may play an important role in the pathogenesis of COPD.\(^1\) Oxidative stress leads to the formation of isoprostanes by the free radical-catalyzed peroxidation of arachidonic acid.\(^3\) 8-isoprostane, a member of the F2 isoprostane class, is increased in urine\(^4\) and in exhaled breath condensate (EBC) of stable COPD patients who are current smokers when compared to healthy smokers.\(^5\)

Patients with COPD have increased neutrophils and macrophages in the bronchoalveolar lavage fluid (BALF) in comparison to healthy control subjects.\(^6\)–\(^7\) More neutrophils are found in induced sputum of COPD patients than in normal subjects,\(^8\)–\(^9\) whereas the number of macrophages is increased 5–10 times in the BALF of patients with COPD.\(^7\)–\(^10\) Chemokines are very small molecules with a molecular weight of about 8 kDa and are a family of cytokines with strong chemoattractant properties. Specific chemokines may be involved in the influx of inflammatory cells into the airway.

Growth-related oncogene (GRO\(\alpha\)) is a CXC chemokine and is first described as a mitogen for human melanoma cells.\(^11\) It is a powerful activator for neutrophils and has chemotactic ability for T-lymphocytes, basophils and neutrophils.\(^11\)–\(^13\) It is produced by different cells including monocytes, endothelial cells, epithelial cells and alveolar macrophages.\(^14\)–\(^16\) It would be detected in the BALF in human lungs.\(^17\) Monocyte chemoattractant protein-1 (MCP-1) is a 8.7 kDa CC chemokine that induces chemotaxis of human monocytes/macrophages and a subset of human T-lymphocytes.\(^18\)–\(^20\) It is produced by monocytes, T-lymphocytes, fibroblasts, endothelial cells and smooth muscles cells.\(^21\)–\(^22\) Previous studies have found that patients with chronic bronchitis have higher MCP-1 in the BALF than healthy non-smokers.\(^23\) In bronchial biopsy specimens, MCP-1 mRNA bronchiolar epithelium expression, including the expression of its receptor (CCR2 in macrophages), was increased in COPD patients when compared to subjects without COPD.\(^22\) The level of GRO\(\alpha\) and MCP-1 in sputum samples, but not BALF, of smoking COPD patients were also increased when compared to non-smokers and healthy smokers.\(^24\) These chemokines may contribute to the inflammatory load associated with COPD.

Our group has demonstrated that T cell-specific chemokines, like macrophage-derived chemokine, could be measured in the EBC of paediatric asthmatic subjects with higher levels than the controls.\(^25\) Eotaxin, one of the major chemotactic factors for eosinophils, could also be measured in virtually all subjects. However, it is not sure whether chemokines related to neutrophilic and monocytic inflammation like GRO\(\alpha\) and MCP-1 can be detected in the EBC of COPD patients.

The aim of this study is to assess the level of oxidative stress and inflammation in the airway non-invasively by collection of EBC. The levels of 8-isoprostane, GRO\(\alpha\) and MCP-1 were measured in both COPD patients and controls and the relationship between their levels, lung function and dyspnoea score was assessed.

Materials and methods

Study population

Thirty-two COPD patients were recruited from the respiratory clinic and the general medical clinic of the Prince of Wales Hospital, Hong Kong. All the subjects had a diagnosis of COPD according to the Global Initiative of Obstructive Lung Disease Guideline\(^26\) and were on bronchodilator treatment. In addition, all their previous lung function studies did not show significant reversibility to bronchodilator (forced expiratory volume in 1 s (FEV\(_1\)) increased by less than 200 ml and 15% of baseline value after 400 mcg of salbutamol). Their chest radiographs also showed no obvious radiographic evidence of fibrosis or bronchiectatic changes. All these patients were ex-smokers (at least 3 months) with at least 10 pack years of smoking history. All patients were not on aspirin, non-steroidal anti-inflammatory agents or systemic steroids. They also had neither intercurrent infection nor exacerbation,
and there was no change of medications for the airway disease for at least 8 weeks prior to the study. Age and sex matched non-smoking subjects with no known chronic respiratory diseases and recent respiratory symptoms for at least 8 weeks were recruited as controls. These control subjects were participants of another project in our unit. They were healthy non-smoking persons from the community who were selected by random telephone digit dialing and invited to have lung function assessment.

The study protocol was approved by the Research Ethics Committee of the Chinese University of Hong Kong and each subject had given informed written consent.

Lung function, 6 min walk test and dyspnoea score measurement

Spirometry (Vitalograph, Model S, UK) was performed on all subjects to determine their lung function according to the American Thoracic Society (ATS) standards. FEV₁ and forced vital capacity (FVC) were measured pre- and postbronchodilator therapy (salbutamol 400 mcg). A 6-min walk test was performed after spirometry according the ATS guidelines. The subjective degree of dyspnoea after the 6-min walk test was assessed by the Borg score (score from 0 to 10).

Collection of exhaled breath condensate

EBC was collected using the EcoScreen (Jaeger, Germany) according to manufacturer instructions. The collection was done from 9 to 10 am in the morning. After rinsing their mouth, the recruited subjects breathed tidally through a mouthpiece that was connected through a unique one-way valve into a cooled collection tube where vapors, aerosols and moisture in the breath condensed along the walls of the tube. The design of the system prevents salivary contamination of EBC. Each subject was asked to breathe through the collection kit for 10 min while wearing a noseclip with more than 1 ml of EBC collected. EBC was stored immediately at −70 °C until analysis.

Measurement of 8-isoprostane, MCP-1 and GROα

The concentrations of 8-isoprostane, MCP-1 and GROα in the frozen EBC were measured in one batch. Concentrations of these markers were measured by sandwich enzyme immunoassays (8-isoprostane from Cayman Chemical, Ann Arbor, MI, USA; MCP-1 and GROα from R & D Systems, Minneapolis, MN, USA) according to instructions provided by the manufacturers. The specificity of 8-isoprostane assay was 100%. The intra-assay and inter-assay variabilities of 8-isoprostane, MCP-1 and GROα were <10%. The sensitivities of this method for 8-isoprostane, MCP-1 and GROα were 4, 5 and 10 pg/ml, respectively.

Assessment of reproducibility of the exhaled chemokine and 8-isoprostane measurements

Intra-subject reproducibility of 8-isoprostane, MCP-1 and GROα was assessed by collection of EBC in healthy volunteers working in the investigator’s laboratories. A total of 10 subjects had EBC collected as described above at the same time (09:00 to 10:00) for 2 consecutive days. All subjects had no known respiratory disease and were free from symptoms of respiratory tract infection or medication use at least 4 weeks prior to study.

Statistical analysis

Data were analyzed by the Statistical Package of the Social Science (SPSS) Statistical software for Window version 11.5 (SPSS Inc, Chicago, IL, USA). Demographic data of the subjects were presented as means ± standard deviation (SD). The 8-isoprostane, GROα and MCP-1 levels were expressed as median and interquartile range (IQR). When their levels were below the detection limit of the sandwich enzyme immunoassay kits, half of the values of the lower detection limit would be taken for statistical analysis. A P-value <0.05 was considered as statistically significant. The 8-isoprostane, GROα and MCP-1 levels were compared between the COPD patients and control groups by Kruskal–Wallis test or Mann–Whitney rank sum test as appropriate. Correlation of lung function, symptoms and peripheral white cell count with the levels of exhaled breath markers were assessed by Spearman’s rank correlation test. Bland and Altman’s method was used to assess repeatability of 8-isoprostane, GROα and MCP-1 in the EBC.

Results

Demographic data of the patients are shown in Table 1. Patients with COPD were divided into two groups. Group 1 had mild-to-moderate COPD with FEV₁ ≥50% predicted. Group 2 COPD had severe COPD with FEV₁ <50% predicted normal. Among the COPD patients, 21 (66%) and 11 (34%) were on
inhaled corticosteroid (ICS) and oral theophylline treatment, respectively. For those patients who were on ICS, the mean daily beclomethasone equivalent dose was 1371.4 ± 754.0 mcg. Group 1 COPD patients had a similar 6 min walk distance as the Group 2 COPD patients ($P = 0.06$). However, the Borg score was much higher in the Group 2 when compared with the Group 1 COPD patients ($P < 0.001$). None of our subjects were on long term oxygen therapy. The mean (SD) of the duration of smoking cessation was 8.6(10.3) years.

The median [IQR] 8-isoprostane level in EBC of COPD patients and controls were 14.2 [9.5–26.4] and 6.0 [4.2–9.7] pg/ml, respectively, with a higher level in the COPD patients than controls ($P < 0.001$). The data are shown in Fig. 1. Patients with more severe COPD (Group 2 COPD) had a higher level of 8-isoprostane (19.3 [12.0–39.5] pg/ml) in the EBC when compared to those with mild-to-moderate COPD (Group 1 COPD) (12.5 [7.1–19.2] pg/ml, $P = 0.045$). 8-isoprostane level did not differ among the COPD patients who were on ICS when compared to those who were steroid naive (19.0 [10.7–40.0])

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**Table 1** Demographics of the COPD and control subjects.

<table>
<thead>
<tr>
<th></th>
<th>All COPD patients ($n = 32$)</th>
<th>COPD patients with FEV$_1$ ≥ 50% predicted (Group 1 COPD) ($n = 14$)</th>
<th>COPD patients with FEV$_1$ &lt; 50% predicted (Group 2 COPD) ($n = 18$)</th>
<th>Control subjects ($n = 18$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>72 ± 9</td>
<td>72 ± 6</td>
<td>72 ± 11</td>
<td>73 ± 5</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>28/4</td>
<td>13/1</td>
<td>15/3</td>
<td>13/5</td>
</tr>
<tr>
<td>FEV$_1$ (l)</td>
<td>0.97 ± 0.49*</td>
<td>1.39 ± 0.45*</td>
<td>0.65 ± 0.17</td>
<td>1.95 ± 0.43</td>
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<tr>
<td>FEV$_1$/predicted (%)</td>
<td>51.5 ± 22.4*</td>
<td>72.2 ± 16.1*</td>
<td>35.3 ± 9.5</td>
<td>121.6 ± 21.3</td>
</tr>
<tr>
<td>FVC (l)</td>
<td>1.73 ± 0.65*</td>
<td>2.13 ± 0.66*</td>
<td>1.42 ± 0.45</td>
<td>2.22 ± 0.50</td>
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<td>FVC % predicted (%)</td>
<td>64.5 ± 19.3*</td>
<td>78.3 ± 17.5*</td>
<td>53.8 ± 12.9</td>
<td>97.2 ± 17.6</td>
</tr>
<tr>
<td>FEV$_1$/FVC</td>
<td>55.9 ± 15.0*</td>
<td>65.7 ± 11.0*</td>
<td>48.3 ± 13.4</td>
<td>87.8 ± 4.1</td>
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<td>Smoking habits (pack-year)</td>
<td>41.5 ± 24.3*</td>
<td>34.8 ± 19.2</td>
<td>45.6 ± 27.0</td>
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<tr>
<td>Duration of smoking (year)</td>
<td>8.6 ± 10.3</td>
<td>8.9 ± 8.4</td>
<td>8.4 ± 11.6</td>
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</tr>
<tr>
<td>BMI (kg/m$^2$)</td>
<td>22.8 ± 4.6*</td>
<td>23.7 ± 4.1</td>
<td>22.0 ± 4.9</td>
<td>25.6 ± 2.2</td>
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<td>Blood neutrophil count</td>
<td>4.98 ± 2.36</td>
<td>4.14 ± 1.37</td>
<td>5.63 ± 2.77</td>
<td>4.03 ± 1.24</td>
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<tr>
<td>( × 10$^9$/l)</td>
<td></td>
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<tr>
<td>Blood eosinophil count</td>
<td>0.28 ± 0.22</td>
<td>0.27 ± 0.18</td>
<td>0.29 ± 0.25</td>
<td>0.17 ± 0.15</td>
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<tr>
<td>( × 10$^9$/l)</td>
<td></td>
<td></td>
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<tr>
<td>Blood monocyte count</td>
<td>0.54 ± 0.21</td>
<td>0.53 ± 0.23</td>
<td>0.55 ± 0.19</td>
<td>0.46 ± 0.18</td>
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<tr>
<td>( × 10$^9$/l)</td>
<td></td>
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<tr>
<td>6 min walk test (m)</td>
<td>288.3 ± 113.5</td>
<td>314.1 ± 132.8</td>
<td>268.2 ± 95.0</td>
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<td>Borg score</td>
<td>4.0 ± 3.4*</td>
<td>1.4 ± 2.4*</td>
<td>6.1 ± 2.5</td>
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</tr>
<tr>
<td>ICS use (n)</td>
<td>21*</td>
<td>8</td>
<td>13</td>
<td>0</td>
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<tr>
<td>Theophylline use (n)</td>
<td>11*</td>
<td>4</td>
<td>7</td>
<td>0</td>
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</tbody>
</table>

Data were presented as mean ± so.

* $P$ value < 0.05 between COPD, and control groups

**Figure 1** The level of 8-isoprostane in the exhaled breath condensate of COPD and control subjects. Group 1: COPD patients with FEV$_1$ ≥ 50%, Group 2: COPD patients with FEV$_1$ < 50%, For Group 1 and Group 2, non-filled symbols represent those not on inhaled corticosteroid and filled symbols represented those on inhaled corticosteroid—— median level, ———— line represents the detection limit of 8-isoprostane.
pg/ml for those on ICS and 12.6 [7.4–19.1] pg/ml in the steroid naive group, *P* = 0.09. 8-isoprostane level in EBC did not correlate with FEV₁/FVC ratio (*r* = −0.27, *P* = 0.14), FEV₁ percentage predicted values (*r* = −0.31, *P* = 0.08), 6 min walk distance (*r* = 0.07, *P* = 0.72) and the degree of dyspnoea as measured by the Borg score (*r* = 0.29, *P* = 0.12) in COPD patients. However, if control subjects and COPD subjects were all included in the analysis, 8-isoprostane value showed a negative correlation with the FEV₁%/ predicted value (*r* = −0.51, *P* < 0.001).

The median [IQR] GROα level was lower in the EBC of COPD subjects than controls (45.4 [44.5–46.2] pg/ml versus 46.0 [45.6–47.3] pg/ml respectively, *P* = 0.02). The data are illustrated in Fig. 2. There was no significant difference in EBC GROα levels between Group 1 and Group 2 COPD patients (45.3 [44.5–46.5] pg/ml versus 45.4 [44.5–46.0] pg/ml respectively, *P* = 0.92). COPD patients who were on ICS therapy did not differ in their EBC GROα level when compared to the steroid naive patients (45.8 [44.5–46.4] pg/ml in ICS group versus 45.3 [44.5–45.5] pg/ml in steroid naive group, *P* = 0.20). EBC GROα level in COPD patients did not correlate with the FEV₁/FVC ratio (*R* = −0.02, *P* = 0.91), FEV₁ percentage predicted value (*r* = −0.146, *P* = 0.43), Borg score (*r* = −0.09, *P* = 0.66) or 6 min walk distance (*r* = −0.35, *P* = 0.06).

The median [IQR] MCP-1 level in EBC did not differ between patients with COPD and controls (5.7 [5.3–6.4] pg/ml versus 5.7 [5.5–6.4] pg/ml respectively, *P* = 0.94). The data are shown in Fig. 3. Patients on ICS therapy did not differ in their EBC MCP-1 levels when compared to steroid naive COPD patients (6.0 [5.3–6.5] pg/ml versus 5.6 [5.3–6.4] pg/ml, respectively, *P* = 0.50). In COPD patients, MCP-1 level in EBC correlated with FEV₁/FVC ratio (*r* = −0.48, *P* = 0.01), but not with FEV₁ percentage predicted value (*r* = −0.18, *P* = 0.32),

**Figure 2** The level of GROα in the exhaled breath condensate of COPD and control subjects. Group 1: COPD patients with FEV₁ ≥50%, Group 2: COPD patients with FEV₁ <50%, For Group 1 and Group 2, non-filled symbols represent those not on inhaled corticosteroid and filled symbols represented those on inhaled corticosteroid. NS: no statistical significance, —— median level, ——— line represents the detection limit of GROα.

**Figure 3** The level of MCP-1 in the exhaled breath condensate of COPD and controls subjects. Group 1: COPD patients with FEV₁ ≥50%, Group 2: COPD patients with FEV₁ <50%, For Group 1 and Group 2, non-filled symbols represent those not on inhaled corticosteroid and filled symbols represented those on inhaled corticosteroid. NS: no statistical significance, —— median level, ——— line represents the detection limit of MCP-1.

**Figure 4** The relationship between MCP-1 level and FEV₁/FVC ratio of lung function in COPD subjects.
Borg score \((r = 0.07, P = 0.72)\) or 6 min walk distance \((r = -0.12, P = 0.51)\). The relationship of MCP-1 level with FEV\(_1\)/FVC ratio is illustrated in Fig. 4.

There was no correlation between the EBC levels of 8-isoprostane, GRO\(\alpha\) and MCP-1. The EBC levels of 8-isoprostane, GRO\(\alpha\) and MCP-1 did not correlate with the differential white cell count in the peripheral blood of COPD patient except that 8-isoprostane correlated with the absolute monocyte count in peripheral blood \((r = 0.51, P = 0.01)\) and the data are shown in Fig. 5.

Ten healthy adults (5 males and 5 females) aged 23–38 years had EBC collected and measured for repeatability testing of the biomarkers. The differences between the majority of the paired measurements laid within \(\pm 2\ SD\) (mean differences 
\[-0.03 \pm 0.32, 1.31 \pm 2.16, -0.46 \pm 1.16\] pg/ml for 8-isoprostane, GRO\(\alpha\) and MCP-1, respectively). The

**Figure 5** The relationship between 8-isoprostane level and absolute monocyte count in peripheral blood of COPD subjects.

**Figure 6** Bland and Altman’s Plot of the repeatability of 8-isoprostane, GRO\(\alpha\) and MCP-1 in the exhaled breath condensate of controls.
coefficients of variation for 8-isoprostane, GROα and MCP-1 were 6.7%, 2.6% and 10.6%, respectively. Bland and Altman’s plots of the repeatability tests are shown in Fig. 6.

Discussion

This prospective, cross-sectional study has shown that ex-smoking subjects with more severe COPD, as reflected by FEV1 of <50% predicted value, had a higher level of 8-isoprostane level in EBC than subjects with less severe COPD. We have also demonstrated that the neutrophilic and monocytic chemokines GROα and MCP-1 could be detected in human EBC.

Our study concurred with previous studies that 8-isoprostane was raised in the EBC of COPD patients who were ex-smokers and current smokers when compared to controls. Kostikas et al. found that the level of 8-isoprostane was higher in the EBC of COPD patients who were current smokers than the smoking controls without COPD. In contrast to our study, Kostikas et al. did not find a difference in the EBC 8-isoprostane level in patients with different severity of COPD stratified according to the FEV1% predicted value. As currently smoking COPD subjects were assessed in Kostikas’ study, it was possible that continuous exposure to cigarette smoke created an environment of high oxidative stress and thus a high 8-isoprostane level in the airway of COPD subjects with different spectrum of disease severity. A previous study also suggested that current healthy smokers without COPD had a higher level of exhaled 8-isoprostane than healthy non-smokers. Apart from cigarette smoking, a recent study found that oxygen therapy, even as short as an hour in duration, raised the oxidative stress in the airway as reflected by the high exhaled 8-isoprostane and IL-6 values. In this current study, ex-smoking COPD subjects, without the continuous stimulation by oxygen or ingredients in cigarette smoke, demonstrated a higher oxidative stress in the airway, in the more severe COPD patients as compared to the mild-to-moderate cases. The level of 8-isoprostane in our COPD patients was lower when compared to previous study. In this current study, ex-smoking COPD subjects had a level of 8-isoprostane at the order of 10–20 pg/ml instead of about 40 pg/ml as in the study by Montuschi et al. There was some evidence to suggest that deficiency of anti-oxidant defenses was related to the degree of airflow obstruction in patients with COPD and plasma levels of anti-oxidants were found to decrease during periods of COPD exacerbations. It is however unclear why oxidative stress in the airway was higher in patients with poorer lung function or whether anti-oxidants help improve lung function of these ex-smoking COPD patients.

This is the first study to demonstrate that chemokines, like GROα and MCP-1, could be detected in the EBC of COPD and normal subjects. We have also demonstrated that GROα and MCP-1 could be measured in the EBC with good reproducibility in control subjects. Cells such as neutrophils and monocytes are involved in the airway inflammation in COPD patients. GROα and MCP-1 are the chemokines involved in the recruitment of neutrophils and monocytes. Their small molecular weight is likely the reason that they can be detected in the EBC. Previous studies reported that both GROα and MCP-1 level were increased in induced sputum, but not in BALF, of currently smoking COPD patients in comparison to healthy smoking and non-smoking controls. Our study on the EBC GROα level in contrast has revealed that its level was marginally lower in ex-smoking COPD patients than that of non-smoking controls. GROα is a potent growth promoting chemokine which is involved in processes like keratinocyte proliferation and angiogenesis. Witherden et al., in their study of human bronchial biopsy specimen, found that cigarette smoke extract suppressed GROα in alveolar type II epithelial cell culture. Previous studies on CXCR2 knockout mice and damaged human tissue suggested that GROα and IL-8 probably played a role in growth and repair processes of the lung. In ex-smoking COPD subjects, other uncertain mechanisms, in addition to the effect of cigarette smoke, may be operating in the airway to suppress the repairing process of lung tissue and contribute to a persistent inflammation in the airway.

It is interesting to note that MCP-1 levels in the EBC from COPD patients correlated with the degree of airflow obstruction as measured by FEV1/FVC ratio in this study. There are conflicting results in the literature about the level of MCP-1 in the airway. Capelli et al. reported that MCP-1 was increased in the BALF of chronic bronchitic patients. However, the same observation was not detected by Traves et al. Increased MCP-1 was noted in the induced sputum of smoking COPD patients. In bronchiolar epithelial cells from resected lung specimens, IL-8, macrophage inflammatory protein-1α, and MCP-1 mRNA levels were higher in smokers with COPD than never-smokers or smokers without either airflow limitation or emphysema. MCP-1 mRNA expression in bronchiolar epithelial cell of lung tissue correlated with its receptor CCR2 expression on macrophages and
mast cells. The assessment of constituents in EBC, induced sputum, BALF and biopsy samples different compartments in the lungs and among these methods, EBC seems a promising tool due to its non-invasive nature. In the assessment of BALF, sampling method including the volume of saline used, may affect the yield of MCP-1 from the alveoli and thus may not be a reliable tool for assessment of chemokines in the airway. More studies are needed to assess the role of MCP-1 in the airway inflammation of COPD patients.

Previous studies found that ICS therapy in COPD patients could not suppress the oxidative stress as measured by 8-isoprostane in the EBC. In this study, it was observed that ICS therapy in ex-smoking COPD subjects could not suppress the oxidative stress, neutrophils and monocytes-related chemokines as measured by levels of 8-isoprostane, GROα and MCP-1 in the EBC. This finding is expected as it is known that ICS therapy does not modify the rate of decline in lung function in all COPD patients and ICS is not recommended for stable COPD patients apart from those with poor lung function and repeated exacerbations.

One major limitation of this study was that we relied on the patients’ self-reported smoking status. Neither urine cotinine level nor exhaled carbon monoxide level was assessed. As a result, ex-smoking status of the patients could not be fully ascertainment.

In conclusion, in this study of the EBC collected from ex-smoking COPD subjects, we have shown that 8-isoprostane level was higher in patients with more severe COPD (FEV₁ <50% predicted) than mild-to-moderate cases. The result suggests there is more oxidative stress in patients with more severe COPD and poorer lung function. The neutrophilic and monocytic chemokines (GROα and MCP-1) could be measured in the EBC. ICS had no effect on the airway inflammatory markers measured in this study. Further studies are needed to assess the role of chemokines in the pathogenesis of COPD.

Acknowledgement

We would like to thank Miss Mabel Tong and Miss Doris Chan for helping with the lung function assessment and 6 min walk test.

References


