Significance of selenium levels in non-small cell lung cancer patients: A comparative study

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Received 8 June 2014; accepted 10 July 2014
Available online 28 July 2014

Abstract Selenium is an essential trace element with potent antioxidant activity. It is a natural health product widely used in the treatment and prevention of lung cancers.

Aim of study: To assess the selenium levels in the epithelial lining fluid, broncho-alveolar lavage and in the serum of non small cell lung cancer patients in comparison with a healthy smoker group and a healthy non smoker group as the control group.

Subjects and methods: Fifty candidates participated in this work. They were classified into; 20 patients with non small cell lung cancer, 15 healthy smoker subjects and 15 healthy non smoker subjects as the control group.

Results: The serum level of selenium was highly significantly lower in non small cell lung cancer patients compared with healthy smokers and healthy non smoker individuals (48.5 ± 9.2, 72 ± 14 and 87 ± 11.3 respectively, \( P < 0.001 \)). The BAL level of selenium was highly significantly lower in non small cell lung cancer patients compared with healthy smokers and healthy non smoker individuals (1.95 ± 0.42, 2.02 ± 0.3 and 2.69 ± 0.2 respectively, \( P < 0.001 \)). Also, the mean concentration of selenium in the epithelial lining fluid was highly significantly lower in non small cell lung cancer patients compared with healthy smokers and healthy non smoker individuals (230 ± 16.4, 289 ± 11.2 and 375.06 ± 15 respectively, \( P < 0.001 \)).

Conclusion: Lower levels of selenium in the serum, BAL and ELF were associated with non small cell lung cancer and to a lesser extent with smokers compared with non smoker healthy individuals.

Introduction

Lung cancer is the most common cause of cancer death in the world, and an estimated 1.04 million new cases occur worldwide each year [1]. Smoking is clearly the most common cause of this disease, but factors such as occupational exposures,
household radon, and certain dietary constituents may also have important impacts on lung cancer risks [2].

Given this, a large number of epidemiologic studies have been undertaken to identify potential risk factors for cancer, among which the association with trace elements has received considerable attention [3].

Reduction of oxygen (occurring in all aerobic organisms), results in the formation of reactive oxygen species (ROS), such as hydrogen peroxide, hydroxyl radicals and superoxide. These are directly responsible for the detrimental effects of “oxidative stress” which is a consequence of a disturbance in the balance between reactive oxygen species (ROS) and endogenous antioxidant defenses, leading to oxidation of lipids, proteins, and DNA in ways that impair cellular functions [4].

Generation of reactive oxygen species is linked to a variety of environmental factors like ultraviolet radiation, cigarette smoking, and alcohol consumption. To counteract the effects of ROS in vivo, there are a number of distinct antioxidant mechanisms in place within the cell, such as superoxide dismutase, catalase, ascorbic acid, glutathione, and selenium [5].

Selenium is an essential trace element with potent antioxidant activity mediated through its ability to increase the activity of the glutathione peroxidase enzymes. Selenium has long been regarded as possessing anticancer effects based on early experiments from the early 1900s that showed regression of carcinoma and sarcoma in vivo [6]. It takes part in a system converting aggressive oxidation products, intracellular free radicals, into less reactive or neutral components [7].

This work aims to assess the selenium levels in the epithelial lining fluid, bronchoalveolar lavage and in the serum of non small cell lung cancer patients in comparison with a healthy smoker group and a healthy non smoker group as the control group.

Subjects and methods

This study was conducted at the Chest Department, Ain Shams University hospitals from June 2013 to January 2014. Fifty candidates participated in this work. They were classified into; 20 patients presented as suspicious cases of lung cancer and proved by investigations to have non small cell lung cancer, 15 healthy smoker subjects and 15 healthy non smoker subjects as the control group.

All candidates were subjected to the following:

- Full history taking.
- Thorough clinical examination.
- Routine laboratory investigations.
- CXR and CT chest.

Biological samples

Blood sample collection and handling

Venous blood (5 mL) was withdrawn and collected in plain vacutainers, the separated sera were divided into two aliquots. The first aliquot was used for the assay of serum urea. The second aliquot was collected in plain vacutainers and stored at −20 °C for selenium determination with Inductively Coupled Plasma (ICP) spectroscopy (Perkin Elmer Optima 4300, DV, USA).

Bronchoalveolar lavage fluid (BAL)

Atropine 1 mg was injected intramuscularly 60 min before bronchoscopy was done, and local anesthesia of the upper airways was given using lignocaine spray 10%, then vocal cords, trachea, main carina, and the two main bronchi were anesthetized using one milliliter aliquots of lignocaine 2% solution. The flexible bronchoscope was wedged in a sub segment of the middle lobe, and five serial infusions and aspirations were performed, each of 20 mL sterile saline (0.9% sodium chloride).

The fluid recovered was collected in polyethylene tubes kept on ice. The recovered fluid was measured and filtered through two single layers of sterile gauze and centrifuged at 500 rpm for 10 min at 4 °C in order to separate the cellular constituents.

Epithelial lining fluid volume (ELF)

The volume of ELF was calculated by the following formula:

$$\text{ELF volume (ml) = BAL urea/sera urea × recovered BAL volume (ml)}$$

Concentrations of urea in BALF and serum were determined by a BM- Hitachi 911 automated analyzer with the original kits of Boehringer-Mannheim based on the urease method [9]. The dilution factor obtained was used to calculate selenium concentrations in ELF.

The healthy smoker and non smoker groups were undergoing fiber-optic bronchoscopy for foreign body extraction.1

Statistical analysis

Data were collected, tabulated and statistically analyzed. All statistical procedures were carried out using SPSS version 15 for Windows (SPSS Inc, Chicago, IL, USA).

Results

The current study was conducted on 50 candidates. They were classified into; 20 patients with non small cell lung cancer, 15 healthy smoker subjects and 15 healthy non smoker subjects as the control group.

The serum level of selenium was highly significantly lower in non small cell lung cancer patients compared with healthy smokers and healthy non smoker individuals (48.5 ± 9.2, 72 ± 14 and 87 ± 11.3 respectively, $P < 0.001$) (Table 1 and Fig. 3).

The BAL level of selenium was highly significantly lower in non small cell lung cancer patients compared with healthy smokers and healthy non smoker individuals (1.95 ± 0.42, 2.02 ± 0.3 and 2.69 ± 0.2 respectively, $P < 0.001$) (Table 1 and Fig. 2).

The BAL level of selenium was highly significantly lower in non small cell lung cancer patients compared with healthy smokers and healthy non smoker individuals (1.95 ± 0.42, 2.02 ± 0.3 and 2.69 ± 0.2 respectively, $P < 0.001$) (Table 1 and Fig. 2).

On comparing the studied groups together, the healthy smoker group showed a significantly lower levels of selenium in the serum, BAL and ELF (72 ± 14, 2.02 ± 0.3, 289 ± 11.2 respectively) compared with these levels in the healthy non smoker group (87 ± 11.3, 2.69 ± 0.2 and 375.06 ± 15 respectively).

1 An informed consent was obtained from each subject.
The non small cell lung cancer patients showed a significantly lower levels of selenium in the serum, BAL and ELF (48.5 ± 9.2, 1.95 ± 0.42 and 230 ± 16.4 respectively) compared with these levels in the smoker and non smoker healthy groups (Fig. 4).

All groups were matched together as regards age and sex with no statistical significant difference between them.

**Discussion**

In the current study we aimed to assess the selenium levels in the epithelial lining fluid, broncho-alveolar lavage and in the serum of non small cell lung cancer patients in comparison with a healthy smoker group and a healthy non smoker group as the control group.

In the present study the serum level of selenium was significantly lower in the non small cell lung cancer group in comparison with the smoker healthy group and the non smoker healthy group (48.5 ± 9.2 μg/ml, 72 ± 14 μg/ml and 87 ± 11.3 μg/ml respectively, *P* < 0.001) and the serum level of selenium was lower in the healthy smoker group than in the healthy non smoker group.

This coincides with another research [10] that studied the selenium concentration in whole blood and plasma, as well as in cancerous and tumor-free lung tissue of lung cancer patients. Blood samples were taken from 84 cancer patients and 61 healthy controls. Normal and neoplastic lung tissues

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**Table 1** Selenium levels in serum, BAL and ELF of the studied groups.

<table>
<thead>
<tr>
<th></th>
<th>Selenium μg/ml</th>
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<tbody>
<tr>
<td></td>
<td>Serum</td>
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<tr>
<td>Healthy non smokers</td>
<td></td>
</tr>
<tr>
<td>Min</td>
<td>47</td>
</tr>
<tr>
<td>Max</td>
<td>122</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>87 ± 11.3</td>
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<tr>
<td>Healthy smokers</td>
<td></td>
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<tr>
<td>Min</td>
<td>45</td>
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<tr>
<td>Max</td>
<td>105</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>72 ± 14</td>
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<tr>
<td>Change%</td>
<td>82.7</td>
</tr>
<tr>
<td><em>P</em> &lt;</td>
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<tr>
<td>Cancer patients</td>
<td></td>
</tr>
<tr>
<td>Min</td>
<td>35</td>
</tr>
<tr>
<td>Max</td>
<td>52</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>48.5 ± 9.2</td>
</tr>
<tr>
<td>Change%</td>
<td>48.5</td>
</tr>
<tr>
<td><em>P</em> &lt;</td>
<td>0.001</td>
</tr>
</tbody>
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**Figure 1** The mean level of ELF selenium in different studied groups.

**Figure 2** The mean level of BAL Selenium.

**Figure 3** The mean level of serum selenium in different studied groups.
were obtained from 57 patients at the time of surgery. Selenium concentrations in whole blood and plasma were lower by 23% \( (P < 0.001) \) in patients compared with controls. On the other hand, the tumor selenium level was higher by 66.6% \( (P < 0.0001) \) than that in adjacent tumor-free tissue. In the whole blood and plasma of cancer patients significantly lower selenium concentrations were found in smokers than in non-smokers. Significantly lower selenium concentrations were also found among cancer patients who were smokers compared with controls. They stated that the cause of increased selenium in the malignant part of the lung is not understood and requires further studies.

This also coincides with a case-control study conducted in a region of north western Poland, on 86 cases of lung cancer, 87 cases of laryngeal cancer and an equal number of healthy controls and studied the serum level of selenium. They found that among lung cancer cases, the mean selenium level was 63.2 \( \mu g/l \), compared with a mean level of 74.7 \( \mu g/l \) in their matched controls \( (P < 0.0001) \) [11].

It also agrees with another study which suggested that low selenium status may be associated with increased risk of lung cancer [12].

In another work they stated that individuals with a low serum selenium concentration had an elevated risk of lung cancer and it was pronounced among smokers [13].

However, other authors concluded that there appears to be a differential chemopreventive effect dependent on baseline selenium status, such that selenium supplementation may reduce the risk of lung cancers in populations with lower baseline selenium status but increase the risk of lung cancers in those with higher selenium [16,17].

In agreement with this selenium has been suggested to prevent tumor development by multiple potential mechanisms that impact distinct stages of carcinogenesis. In antioxidant systems, selenium can participate by incorporation as selenocysteine into more than 25 selenoproteins, such as glutathione peroxidase and thioredoxin reductase. Many studies have suggested that selenium may also play a role in minimizing DNA damage as well as augmenting DNA repair capacity [18].

However, other authors concluded that there appears to be a differential chemopreventive effect dependent on baseline selenium status, such that selenium supplementation may reduce the risk of lung cancers in populations with lower baseline selenium status but increase the risk of lung cancers in those with higher selenium [16].

Also, in another study they stated that selenium supplementation did not significantly decrease lung cancer incidence in the full population, but a significant decrease among individuals with low baseline selenium concentrations was observed [19].

**Conclusion**

Lower levels of selenium in the serum, BAL and ELF were associated with non small cell lung cancer and to a lesser extent...
with smokers compared with non smoker healthy individuals. Oxidative stress and antioxidant role of selenium could be a suggested explanation. However, the definite role of selenium and its mechanism in the cancer process are not clear yet. Also, its preventive activity against cancer is controversial. On the other hand, studying the role of selenium and other trace elements and antioxidants in the mechanism of malignancy could provide us with a better understanding to these risk factors and how to overcome.

Conflict of interest

None declared.

References