Association of circulating omentin-1 level with lung cancer in smokers

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Abstract

Background: Omentin has recently been considered as an adipokine secreted from visceral fat and is expressed in the lungs, heart, ovary etc. Various studies have shown that omentin may have an anti-inflammatory role in the inflammatory process and the amount of omentin alters in some cancers, such as colorectal, prostate and renal cells cancers, changes. The serum level of omentin, however, remains unknown in non-patient smokers and the smokers afflicted with lung cancer. Therefore, this study examines the serum levels of omentin in smokers suffering from lung cancer.

Methods: The amount of serum omentin was measured in 45 patients with lung cancer and 61 age- and sex-matched controls (30 smokers and 31 non-smokers) using enzyme-linked immunosorbent assay (ELISA) kit. Data were analyzed using SPSS-16, and one-way analysis of variance and Scheffe post hoc test were used to determine and compare the serum levels of omentin in different types of lung malignancies. Significance level was set at p≤0.05.

Results: The amount of circulating omentin for healthy non-smokers and non-patient smokers was 3.55±0.57 ng/l and 5.43±1.95 ng/l, respectively (p<0.001). The serum level of omentin was 3.63±0.70 ng/l for smokers afflicted with cancer (p<0.001 compared with non-patient smokers: 5.43±1.95).

Conclusion: The meaningful decrease in omentin levels in smokers with lung cancer can be considered as a risk factor in smokers and can use as a significant factor in the prognosis of lung cancer in these people.

Keywords: Smoker, Omentin, Lung cancer

Conflıt of Interests: None declared

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Introduction

Lung cancer is one of the pulmonary diseases and is the uncontrolled growth of the epithelial cells of the lung and its prevalence in smokers is higher as compared to non-smokers. Around the world, lung cancer is the most common cancer in terms of outbreaks and death. In 2012, 1.8 million new items (12.9% of all people with all types of cancers diagnosed in this year) and 1.6 million deaths from lung cancer were reported (1). Being among the five major cancers in Iran, the lung cancer afflicts a large number of people about 80% of which included by smokers (2). Adipose tissue is known as an endocrine and immune organ (3). Until recently, adipose tissue was thought to affect only lipid metabolism and glucose homeostasis. This tissue is now identified as the secretion source of more than 20 types of different hormones and molecules called adipokine or adipokine which play significant biological roles in the vascular system, glucose homeostasis, reproduction, bone metabolism, immune system and cancer (4-5).
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As one of the adipokines, omentin (or intelectin) was first found in the intestinal paneth cells, which reacts with galactofuranose in the carbohydrate part of the cell wall of the bacteria and is involved in intestinal defense mechanisms against pathogenic bacteria (6). Omentin-1 is the type of omentin which is mostly addressed in research papers. There is another homolog of omentin which is called omentin-2. About 83% of its amino acids are identical to that of omentin-1. Omentin 1 is also expressed in the lungs, heart, ovary, and placenta (7-10) and is secreted as a new adipokine in visceral adipose tissue. The Laboratory experiments show that omentin increases the level of insulin sensitivity (i.e. increases the glucose uptake by insulin) (10) and activates Akt signaling pathway. Akt is a serine/threonine protein kinase that plays an important role in multiple cellular actions such as glucose metabolism, cell proliferation and apoptosis as a secondary messenger (7). Also, the increase in omentin leads to a decrease in the level of CRP in serum and decreases the effects of TNF-α (tumor necrosis factor alpha that increases in inflammatory conditions). So there can be a connection between omentin and inflammation (7, 11-12). Chronic inflammation increases the risk of cancer (12), and in some cancers, inflammation occurs before the onset of cancer and malignancy (1, 13). Cigarette smoking causes chronic inflammation in the lungs, and inflammatory mechanisms also cause a lung tumor under the influence of smoking (12).

The amount of gene expression of this adipokine is reduced in the epithelium of smokers' airways (14), and though it is known that omentin is secreted from the epithelial cells of the lung, it is not clear whether there is an increase or decrease in the serum level of this hormone in smokers with lung cancer.

Methods

Study population

The patient group of this study were 45 smoker male patients referred to the pulmonary clinic of the Imam Khomeini hospital in Urmia, Iran. The control group consisted of 61 males with no history of illness and with matched of age and BMI (Body mass index) (30 smokers and 31 non-smokers). The protocol of the study followed the principles of the Declaration of Helsinki. All the subjects signed the informed consent form. Initially, careful lung examinations were conducted and then the tissue biopsy specimens were sent to the histopathology laboratory for more accurate diagnosis. The blood and urine parameters for all the individuals in both groups were within normal ranges.

Laboratory analysis

Before starting any type of therapeutic treatment in patients, peripheral blood was drawn from subjects after measuring their height and weight to calculate BMI. After separation of the serum of the samples in a cooling centrifuge and spinning at 3000 rpm for 10 min, the biochemical parameters such as fasting blood glucose (FBG), triglyceride (TG) and low density lipoprotein – cholesterol (LDL-c) were detected via the standard protocols using a clinical chemistry autoanalyzer (BT 3000, Italy) in the laboratory of Imam Khomeini Hospital in Urmia in the sampling day. Then serum was frozen at −80 °C until the analysis of omentin. Serum omentin was measured using commercially available enzyme-linked immunoassay (ELISA) kits (Bioassay technology laboratory, China) according to manufacturer’s instructions. The sensitivity of the assay was 1.03 ng/l (assay range: 2-600 ng/l). The intra- and inter-assay coefficients of variance were <8% and <10%, respectively.

Statistical analysis

All data were analyzed using the SPSS software package version 16. The results are presented as means ± S.D. The analyses of normally distributed variables (age and BMI and biochemical analysis) were conducted using independent-sample t-test. To determine and compare the serum levels of omentin in different types of lung malignancies, one-way analysis of variance was used and finally, Scheffe post hoc test was used as well. Kolmogorov-Smirnov test were used to determine whether or not they were normally distributed and the analyses of abnormally distributed variables were conducted with the Mann-Whitney U test. Comparisons with p<0.05 were considered to be statistically significant.

Results

The baseline characteristics of the subjects are summarized in Table 1. The mean age in the control group who did not smoke was 58.87±7.19 whereas it was 58.65±7.82 for the smokers in the control group. The mean BMI of these the two groups were 24.58±2.93 and 24.10±2.93, respectively. The mean age of the patient group was 65.13±9.32, and the mean BMI of the patient group was 23.82±4.28. The values of other biochemicals are given in Table 1.

Figure 1 shows the changes in the level of omentin hormone in the healthy and cancerous groups as follows: 3.55 ± 0.57 ng/l for nonsmokers and 5.43±1.95 ng/l for smokers in the control group and 3.63±0.70 ng/l for the patient group.

The amount of serum omentin was different in a variety of pulmonary malignancies. It was 3.04±0.38 ng/l in SCC (squamous cell carcinoma), 4.08±0.31 ng/l in adenocarcinoma, 3.88±0.50 ng/l in small cell carcinoma and 4.27±0.65 ng/l in other lung diseases (for example poorly differentiated carcinoma) according to Figure 2.

Table 1. The baseline characteristics of subjects

<table>
<thead>
<tr>
<th>Variables</th>
<th>Non-smoker, non-patient (n=31)</th>
<th>Smoker, non-patient (n=30)</th>
<th>Smoker, patient (n=45)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>58.87±7.1</td>
<td>58.65±7.8</td>
<td>65.13±9.32</td>
<td>0.061</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.58±2.93</td>
<td>24.10±2.93</td>
<td>23.82±4.28</td>
<td>0.917</td>
</tr>
<tr>
<td>FBS (mg/dl)</td>
<td>81.35±9.58</td>
<td>82.16±9.45</td>
<td>82.32±10.44</td>
<td>0.946</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>95.83±7.91</td>
<td>94.30±8.94</td>
<td>95.86±8.97</td>
<td>0.438</td>
</tr>
<tr>
<td>LDL-c (mg/dl)</td>
<td>79.19±7.73</td>
<td>79.26±9.31</td>
<td>80.13±11.27</td>
<td>0.717</td>
</tr>
</tbody>
</table>

Data are presented as mean±SD. BMI (body mass index), FBS (fasting blood sugar), TG (triglyceride), LDL-c (low-density lipoprotein-cholesterol).

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et al. only OSAS patients without specific comorbidities in-
(such as diabetes, tumors, or alcohol and drug abuse) other
Wang et al. study, cases had no history of any other illness
by Kar Kurt in 2014 showed the opposite result. In the
(obstructive sleep apnea syndrome) patients, while a study
inflammatory factors such as CRP in patients with liver dis-
excretion in renal patients or lack of synthesis of some in-
of omentin in these patients is its defective degradation and
in serum of patients with CAD (coronary artery disease) in
spite of the decrease in the expression of omentin in the ep-
idermal adipose tissue in these patients is due to the secre-
tion of omentin from the macrophages in the atherosclerotic
plaques (20).

Since the discovery of omentin, its role in tumorigenesis
has been shown in a large number of studies. In women
with EEC (Endometrioid Endometrial Cancer) and CAH
(Complex Atypical endometrial Hyperplasia), the levels of
serum omentin decrease in relation to BMI-matched healthy people .EEC is an inflammatory disease that is as-
associated with obesity and diabetes (24). Also, in women
with ovarian cancer the levels of serum omentin decrease.
Besides, the power of proliferation, motility, and cellular
invasion in these cancer cells is reduced by the effect of
omentin (25), So that patients with high serum omentin have a longer life span than those with lower serum omen-
tin. In this case, it is hypothesized that there may be a neg-
eative effect on cell proliferation (24). It has been proved in
various studies that the level of serum omentin increases in
prostate, colorectal and pancreatic adenocarcinoma can-
cers, while it decreases in RCC (Renal Cell Carcinoma) and
Bladder cancer. It seems that increasing the amount of
omentin in some cancers stimulates cell growth by trigger-
ing genomic instability and PI3K/Akt (phosphatidylinosi-
tol-3 kinase downstream effector) signaling pathways
thereby contributing to
the pathogenesis of these cancers (26-29). On the other
hand, omentin plays a major role in inflammatory responses and
acellular differentiation and has a significant contribu-
tion to inducing apoptosis in cancer cells (30-31). Omentin
stimulates apoptosis in cells through the activation of JAK
signaling pathway and P53 upregulation mechanisms (30). It
also inhibits inflammatory diseases via suppression of
JNK (Jun N-terminal kinase) activation through the
AMPK/eNOS (endothelial nitric oxide (NO) synthase) sig-
aling pathway (22). Also omentin reduces the expression
of VCAM-1 (vascular cell adhesion molecule-1) and
ICAM-1 (intercellular cell adhesion molecule-1) (the mole-
cules involved in the pathogenesis of cancer cells) adhe-
sion molecules through inhibition of P38, JNK pathway and
blocking of ERK/NF-κB (extracellular signal-regulated ki-
nase/nuclear transcription factor kappa B) pathway (23, 31).
Another mechanism of omentin in triggering apoptosis

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in cells is increasing the bax/bcl-2 protein ratio and activation of the caspase-3 signaling pathway (30). Therefore, the reduction of omentin in RCC and ECC increases cellular proliferation and decreases apoptosis in cancer cells. In this study, we demonstrated that the circulation of omentin is decreasing in the lung cancer patients and the decrease in its amount in the smoker patients is significant compared to non-patient smokers.

About 85% of the total lung cancer cases were non-small cell lung cancer (NSCLC) which mainly includes squamous cell carcinoma (32) and adenocarcinoma, and these contain approximately 400,000 deaths each year in the world (32-33). Smoking is the main cause (85–90%) of lung cancer in smokers (34), and the prevalence of SCC is more than that of adenocarcinoma in smokers (33). Metastasis and recurrence are very common in SCC (32) and in the invasive types of the tumor with rapid initial growth (35). As shown in this study, the amount of serum omentin in SCC patients decreases more significantly than in patients afflicted with other lung malignancies.

Conclusion

Omentin-1 levels were found to be significantly lower in smoker lung cancer patients, irrespective of their general clinical conditions. These findings suggest that this adipokine might play some crucial role in the tumorigenesis of lung cancer via mechanisms that are active in lung cancer. Thus, the measurement of omentin in smokers may be considered as a significant factor in the prognosis of lung cancer in smokers and should be further investigated.

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Conflict of Interests

The authors declare that they have no competing interests.

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