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Prediction of electron density and trace element concentrations in human blood serum following radioiodine therapy in differentiated thyroid cancer patients

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ABSTRACT

The aim of this study is to investigate trace element levels (Cr, Cu, Fe, Mg, Mn, Se, Zn, As, B, Si and Co) in serum samples of patients with papillary thyroid cancer. The analysis of trace elements levels of samples carried out using ICP-OES. Elements in blood samples were determined by ICP-OES after using Hettich Universal Centrifuge and differences between the values of Zn, Mg, Fe and Cu of blood samples were obtained pre-therapy and post-therapy. The concentrations of elements were normalized to percentage. Later, electron densities (N_{el}) of blood samples have been determined using ZXCOM program. A venture was made to perform a correlation between electron density and pre-posttreatment. This attempt is quite new in literature. Interestingly, it was generally observed that the electron densities of blood samples posttreatment are higher than pretreatment. Among elements, normalized concentration values of Cu and electron densities were in particular compared with patient type. Also, statistical analysis of blood results was achieved for 11 patients and 11 normal individual as control group for pre-posttreatment. Wilcoxon test which is a non-parametric test was used.

1. Introduction

Minerals are extremely important for life. Cancer is the second most important incident disease after cardiovascular system diseases in the World. The factors causing cancer are varied. However, deficiency or excess of some elements might be cause of cancer and other condition risks. Thyroid cancer is a disease in which malignant (cancer) cells form in the tissues of the thyroid gland which is one of the largest endocrine glands in the body and controls the body's sensitivity, rate of use of protein synthesis and energy sources. The cancer is rising over the world and mostly due to an increase in the detection of small tumors that were previously undetected [1]. In 2012, ~40000 deaths from its cause and ~300000 new cases of thyroid cancer were expected worldwide. Recently, new cases of thyroid cancer have been reported at 12.9 per 100000 a year. While the risk of death from thyroid cancer is about 1.1%, 70% of the cases are diagnosed at early stages and resulting in a 5-year survival rate of 97.8%. Thyroid cancer type and incidence are varied in which papillary and/or mixed papillary/follicular thyroid cancer is the highest ~80%, while follicular and/or Hurthle cell thyroid cancer ~15%, and the lowest is Medullary thyroid cancer and Anaplastic thyroid cancer, ~3% and ~2% respectively [2,3].

The pathogenesis of some diseases is associated with the proportional distribution of certain elements [4,5]. Meanwhile, the trace elements are essential for numerous metabolic and physiological processes in the body [6]. Biological molecules and enzymes can modify their reactivity and originate precipitates or complexes with elements involved in the metabolism, and they might act as catalyzer in chemical reactions originating decomposition of necessary metabolites [7]. In humans, deficiency or excess of elements such as Fe, Cu, As, Cr, Be, Cd and Ni was reported to cause liver cancer in hemochromatosis, respiratory tract cancer, urinary tract cancer, and thoracic cancer, skin cancer, lung cancer, and central nervous system tumors, stomach cancer and prostate cancer [8–10]. Therefore, imbalances in the optimum levels of elements may affect biological processes and these levels are associated with

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many diseases including autoimmune disease, cancer, renal failure and neurological disorders [11–13]. Most of the relative diseases may be associated with changes in the balance of elements such as Mg, Cu, Zn and Fe. The elements play an important role in the structural stability and production of both proteins and nucleic acids. Additionally, they are included in the carbohydrates and enzymes. Balance of elements has been explored in many diseases such as cancers, diabetes, cardiovascular diseases, and neurological disorders [12,14,15].

In addition, Boyd et al., reported an association between Fe ore minerals and the incidence of lung cancer [16]. Magalhães et al., also reported a similar pattern for tissues [7]. The results showed an increase in the levels of P, S, K, Ca, Fe, Cu and a decrease in that of Zn, Br, when compared with carcinoma and healthy tissues. Al-Sayer et al., reported measured elements in serum levels of Zn, Cu, Fe, Mg, Se and Mn for thyroid cancer patients before and after surgery compared to blood samples from healthy people. In cancer patients, the serum levels of Zn were lower than those of normal samples. Besides, levels of Fe, Mg and Mn were significantly lower ($p < 0.001$), but Cu levels in serum of patients significantly raised after surgery ($p < 0.001$). There was no significant change in serum Se levels [17]. In another study Zaichick et al., reported that Rb, Hg, Ag, Co and I contents were much higher for thyroid cancer nodules than that of the control group. However, Se levels were slightly lower in the nodules compared with the healthy group [18]. Also, Zhang et al., studied the changing of Zn, Cu, and Fe in serum and erythrocyte from patients with hyperthyroidism before and after $_{131}$I therapy. It was found that there is no significant correlation between erythrocyte and serum [19].

According to the literature, these diseases may be associated with changes in proportional distribution of elements. For instance, Antoniassi et al., reported an electron density of 33 samples of normal (adipose and fibroglandular) and neoplastic (benign and malignant) human breast tissues determined through Compton scattering data. Adipose tissue exhibited the lowest values of electron density (N_{el}) whereas malignant tissue was the highest. Further, the presence of correlation was confirmed between human breast tissues and electron density in several studies [20,21].

Radioactive iodine therapy for differentiated thyroid cancer patients is a standard procedure for ablation of remnant thyroid tissue and metastases after thyroidectomy. Thyroid cancer patients are usually treated with high dose ranges (3700–7400 MBq) to fulfil successive therapy.

One of the most important aspects of this study is to find the correlation between blood serum elements of thyroid cancer disorder and electron density values. Also, the concentrations of elements obtained from inductively coupled plasma optical emission spectrometry (ICP-OES) were normalized to percentage. Later, electron densities of blood samples were determined by means of ZXCOM before and after radioactive iodine administration. An attempt was made to establish a correlation between electron density for a group of patients before and after treatment. This attempt is quite new and to best of our knowledge there is no enough information in literature about this correlation.

2. Experimental

2.1. Instrumentation and measurements of trace elements

Blood serum analysis was performed using ICP-OES (ICAP-6000) in Department of Biophysics of Cerrahpaşa Medical Faculty of Istanbul University. ICP-OES emission spectrometer enclosed with the plus auto sampler was controlled by a computer (Thermo Fisher Scientific Inc., Istanbul, Turkey). ICP-OES was operated under suitable conditions including choosing the suitable wavelength for each element; Cr (267.716 nm), Cu (324.754 nm), Fe (259.940 nm), Mg (285.213 nm), Mn (257.610 nm), Se (196.090 nm), Zn (206.200 nm), As (189.042 nm), B (249.773 nm), Si (251.611 nm) and Co (228.616) respectively. In ICP-OES, the plasma operating conditions: 1.5 L/min sample flow rate and elution flow rate, 15 L/min plasma gas flow rate, 0.5 argon carrier flow rate, peristaltic pump works 100 rpm. The transport lines are a Polytetrafluoroethylene pipe with a diameter of 1.25 mm.

2.2. Reagents

ICP-OES labor standards were prepared from appropriate standard solutions including 1.000 ppm for each tested element obtained from Chem Lab NV located in Zedelgem/Belgium. Reagents with analytical reagent grade and deionized water were used. Stock solutions of Cu, Cr, Mg, Mn, Fe, Se, Si, Co, Zn, B and As were prepared by taking the appropriate standard in deionized water. Solutions were prepared freshly before using doubly distilled deionized water was used in this study. To reduce the risk of contamination from ambient air and dust, all process was performed on a clean bench. All the volumetric flasks used were cleaned soaking in with 10% (v/v) nitric acid (HNO_3) solution during the day before use. These were rinsed with deionized water thoroughly and dried in an oven overnight at 100 °C [22].

2.3. Population

This study was planned according to ethical committee approval from Ethical Committee at Cerrahpaşa Medical Faculty of Istanbul University. 22 individuals attended to the Outpatient Clinic of Department of Nuclear Medicine in Cerrahpaşa Medical Faculty between November-December 2015 were randomly enrolled in the study.

2.4. Experimental design

Serum trace element values of groups are given at Table 1. All the cancer patients were treated with radioiodine therapy. Patients were divided in three groups as pretreatment (Group 1, n = 11), posttreatment (Group 2, n = 11) and control group (Group 3, n = 11). The samples were taken from the cancer patient's pre-posttreatment. Radioactive iodine therapy for differentiated thyroid cancer patients is a standard procedure for ablation of remnant thyroid tissue after thyroidectomy and treatment of persistent disease and metastases. In this study, all the thyroid cancer

Table 1
Trace element values of groups.

Trace elements (ppm)	Pretreatment (n: 11)	Posttreatment (n: 11)	Control groups (n: 11)
Cr	0.011 ± 0.008	0.001 ± 0.002 a***	0.077 ± 0.050 a***. b***
Cu	1.204 ± 0.274	1.177 ± 0.286	1.173 ± 0.273
Fe	0.713 ± 0.225	1.361 ± 0.800 a**	1.053 ± 0.107 a***
Mg	25.928 ± 2.628	25.252 ± 3.781	21.511 ± 2.239 a***. b**
Mn	0.005 ± 0.002	0.002 ± 0.001 a***	0.270 ± 0.122 a***. b***
Se	0.087 ± 0.006	0.084 ± 0.011	0.077 ± 0.012 a*
Zn	1.055 ± 0.145	1.177 ± 0.524	0.872 ± 0.172 a**
As	0.531 ± 0.052	0.995 ± 1.407	0.095 ± 0.016 a***. b*
B	0.019 ± 0.023	0.017 ± 0.011	0.051 ± 0.021 a***. b***
Si	7.284 ± 1.864	9.385 ± 5.349	8.497 ± 2.149
Co	0.005 ± 0.004	0.002 ± 0.000 a*	0.816 ± 0.255 a***. b***

In comparison to the pre-treatment group compared to other groups **a**; posttreatment the comparison group than the other groups **b** It shows statistical significance.
* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.