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STUDY OF TRACE ELEMENTS STATUS OF BREAST CANCER PATIENTS

The last 15 years, the methods of evaluation of trace elements in the human body for the hair analysis have been actively developing. The content of trace elements in hair reflects their level in the human body, and is an integral indicator characterizing his element status. ***Purpose:*** *study of trace elements in patients with second-stage breast cancer.* ***Object and Methods:*** *to determine the content of trace elements, it was studied the hair of 30 patients with stage II breast cancer who were treated at the National Cancer Research Center of the Ministry of Health of the Republic of Uzbekistan in 2016. The study of hair samples for content of trace elements (calcium, potassium, sodium, chlorine, iron, zinc, copper, manganese, cobalt, chromium, selenium, iodine, bromine) was conducted in the laboratory analysis of the activation of the Institute of Nuclear Physics of Uzbekistan Academy of Sciences, instrumental neutron activation analysis. The received data on the micronutrient content in hair of patients compared with reference values for the population of Uzbekistan, adopted at the Institute of Nuclear Physics.* ***Results:*** *the reduction of iron, zinc, copper, cobalt level and high content of chlorine as compared with the reference values were showed.* ***Conclusions:*** *undertaken studies have shown the possibility of using of the results for the primary prevention and identification of risk groups among women, as well as the usefulness of the correction of specialized treatment medication with microelement complexes.*

INTRODUCTION

Breast cancer (BC) is a multifactorial disease. Environmental factors such as radiation, viruses and chemicals have an important role as carcinogenic agents. At the same time, numerous secondary factors: gender, age, economic development of the country of residence, later first birth (40 years and older), the presence of blood relatives diagnosed with BC, ionizing radiation to the chest area, early menarche (under 12 years old), late menopause (after 55 years), breast-feeding, increased body weight in post menopause, sedentary lifestyle, use of oral contraceptives, hormone replacement therapy and dense breast tissue also have a significant effect on the occurrence and the development of breast tumors [1].

Until recently, the main focus of cancer research has been directed at identifying natural or man-made carcinogens. Primarily, to the prevention of cancer came, as a problem removing the newly discovered carcinogens from the environment or minimize the impact of these agents on humans.

Although some progress has been achieved on the basis of this approach, however, it became increasingly apparent that the complete removal of all cancer-causing agents in the environment is impossible. Furthermore, there is a possibility that some malignant tumors develop under the influence of endogenous carcinogenic agents.

Currently, health care workers involved in the prevention of cancer in North America and Europe, pay more and more attention to the ways and means by which the body's resistance could be strengthened sufficiently to resist the effects of carcinogens and other factors, which all people naturally are subject to a greater or lesser extent.

When there are high expectations in the alimentary cancer prevention, because it can be the easiest and most effective way. This area of cancer research is new, where trace elements play an important role. Excess or deficiency in the body of certain chemical elements or their compounds often leads to pathological conditions [2]. Currently, it is known the relationship between chemical composition of biological substrates and concrete manifestations of the pathological process, for example for cancer of the gastrointestinal tract [3]. In the development of tumor process microelements play a dual role — on the one hand, they actively accumulate tumor cells, promoting their proliferation, on the other hand, they are capable of potentiating the antitumor immunity [4, 5]. The role of trace elements in the process of regeneration and differentiation, apoptosis in the pathogenesis of tumor proved literature data [6]. It should be stressed their importance in the regulation of the activity of oxidative stress as one of the pathogenic mechanisms of initiation and support of tumor growth in humans [2].

The last 15 years, the methods of evaluation of trace elements in the human body for the hair analysis has been actively developed. The content of trace elements in hair reflects their level in the human body, and it is an integral indicator characterizing his element status [7]. The hair is most informative biological substrate as compared to others (blood, urine, saliva, lacrimal fluid, etc.), it is simple and fence materials, non-invasive, has long-term storage ability and the higher information content of microelements.

Trace element analysis of human hair makes it possible to assess state of the environment (housing, water, food and so on), that allows carrying out sanitary-epidemiological and preventive measures.

As a result of studying the microelement status it is possible to early prediction of cancer risk in the population, especially in areas with unfavorable ecological situation and the presence of large industrial enterprises with hazardous

production conditions [4, 8, 9]. The hair compared with other biological substrates accumulates the processes having long-term place in the human body under the influence of complex of ecological and physiological factors, so the analysis of the elemental composition can serve as a means of diagnosis and a test to determine predisposition to certain diseases, and also allows to find out the possible causes of inefficient treatment [10, 11].

However, so far in the literature there are only a few fragmentary reports of the multivariate analysis and the content of trace elements in the hair of patients with such common oncological disease as BC [12–14].

The purpose of research is the study of trace elements in the hair of patients with stage II BC.

MATERIALS AND METHODS

To determine the content of trace elements it has been studied the hair of 30 women with stage II BC treated at the National Cancer Research Center of the Ministry of Health of the Republic of Uzbekistan in 2016. In the study, the ethical principles of the World Medical Association Declaration of Helsinki (1964, 2000) were met. A voluntary consent to perform microelement analysis of hair was received from every woman.

The average age of the patients was 50 ± 2,9 years. The disease was confirmed by carrying out clinical, ultrasound, mammography, cytological and histological studies. Biochemical studies were carried out (coagulogram, the study of blood glucose, bilirubin, total protein). The study of hair samples on the content of trace elements (calcium, potassium, sodium, chlorine, iron, zinc, copper, manganese, cobalt, chromium, selenium, iodine, bromine) was conducted in the laboratory activation analysis of the Institute of Nuclear Physics, Academy of Sciences of Uzbekistan tool neutron activation analysis. Methods of preparing and carrying out the instrumental neutron activation analysis are described in detail in [15, 16].

The data given by various authors of the normal range of the content of most of the trace elements in the hair are variable, because different regions are at different levels of anthropogenic load, so the elemental composition of hair of people in each region has its own peculiarity. The concentration of micronutrients in hair composition may vary depending on the race, health condition, diet and hair color [10]. 95% confidence interval (CI) [17] of the received data on the micronutrient content of the in hair of patients compared with reference values for the population of Uzbekistan, received at the Institute of Nuclear Physics, Academy of Sciences of Uzbekistan (Tashkent). Statistical analysis of the results was carried out using MS Excel 2010 and Statistica v. 6 program.

RESULTS AND DISCUSSION

An analysis of the elemental composition of hair clearly demonstrates the presence of imbalance in patients with stage II BC. There is a decrease in the content of iron, zinc, copper, cobalt and to high contents of chlorine. Comparison of the content of trace elements in the hair of patients with BC with normal ranges of contents is shown in Table.

CI of the concentration of calcium, potassium and sodium in the hair of BC patients was within the reference values. Calcium has a direct impact on the energy balance of the body. Changes in rates of cellular transport of adenosine triphosphate dependent on calcium concentration, which may occur in the cells of a malignant tumor [18]. The test results show that the lower bound of CI of chlorine in hair from patients with BC was 51.4% above the upper limit of reference values (3028.0 μg/g).

Considering the physiological role of sodium, potassium and chlorine it should be noted that these elements are the building blocks of all cells and tissues. In the body, they are in a certain ratio to provide a constant internal environment. Sodium and potassium chlorides and strong electrolytes are involved in the generation and conducting electrical pulses and nerve. An excess of potassium and sodium ions causes a change and disturbance of homeostasis of metabolic processes in the body.

The incidence of excess and deficiency of trace elements in the hair of patients with BC relative to the upper and lower reference indicators are presented in Figure.

In determining the copper content in hair of patients with BC it has been proved that the upper bound of CI concentration of this bioelement was 54.0% less compared to the lower limit of reference values (9.2 μg/g). Copper is present in many enzymes (tyrosinase, ceruloplasmin, aminoxidases, cytochrome oxidase), involved in the oxidation.

Table

The content of microelements in the hair of patients with BC, μg/g

Element	Patients with BC (n = 30)			Reference range	
	M ± m	95% CI			
		Lower limit	Upper limit	Lower limit	Upper limit
Calcium	1100.0 ± 280.0	551.2	1648.8	1500.0	2500.0
Potassium	1700.0 ± 220.0	1268.8	2131.2	1000.0	1500.0
Sodium	1700.0 ± 440.0	837.6	2562.4	500.0	900.0
Chlorine	4400.0 ± 700.0	3028.0	5772.0	1000.0	2000.0
Iron	19.0 ± 1.3	16.4	21.5	25.0	40.0
Zinc	110.0 ± 13.0	84.5	135.5	150.0	250.0
Copper	7.5 ± 0.9	5.7	9.2	20.0	35.0
Manganese	0.51 ± 0.04	0.43	0.58	0.40	1.00
Cobalt	0.04 ± 0.01	0.025	0.054	0.07	0.12
Chrome	0.32 ± 0.16	0.006	0.633	0.40	1.00
Selenium	0.38 ± 0.04	0.305	0.454	0.40	1.00
Iodine	6.60 ± 2.80	1.1	12.1	1.00	2.00
Bromine	2.30 ± 0.31	1.69	2.9	1.50	3.50

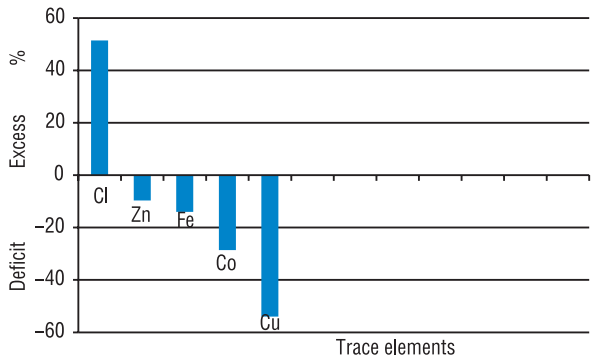

Figure. The incidence of excess and deficiency of trace elements in the hair of patients with BC relative to the upper and lower reference rates

Introduction of copper salts also protects the liver from the damaging effects of a number of carcinogens. However, the copper has a selenium-antagonistic property of selenium deficiency symptoms were obtained in animals treated with high doses of copper. At deficiency of copper under the influence of dimethyl hydrazine in rats there is a high incidence of renal tumors compared to animals that received additional doses of copper [19].

When assessing the content of microelements discovered that patients with BC upper bound CI iron concentration was 14.0% lower than the lower limit of normal values (32.2 μg/g). Iron plays an important role in the processes of energy generation, in enzymatic reactions in achieving immune functions. Iron deficiency leads to dysfunction of the major systems of the body: blood-forming, nervous, immune and adaptation. High concentrations of copper and iron were observed in the liver and spleen in patients with cancer of the respiratory tract, the genitourinary system, and breast. In the tissues of malignant tumors of the esophagus, bronchi, gastrointestinal tract and mammary gland are often increased copper content than in the tissues of benign tumors [20].

The upper boundary of CI the content of zinc in hair of patients with BC was 9.7% below lower limit of reference values (135.5 μg/g). Zinc is an enzyme cofactor of about 80 enzymes and is necessary for growth, development, reproduction, wound healing and other important physiological functions. In those countries, where the food is rich in zinc, cancer mortality is higher than in countries where the national diet zinc content is less. Zinc ions exist primarily in the form of complexes with proteins and nucleic acids and participate in all aspects of intermediary metabolism, transmission and regulation of the expression of genetic information, storage, synthesis and action of peptide hormones and structural maintenance of chromatin and biological membranes. Zinc plays a key role in the synthesis of proteins and nucleic acids. It is involved in the mechanisms associated with the processes of regulation of gene expression. Zinc deficiency is primarily associated with dysfunction of the immune system [21].

The upper bound of CI cobalt concentration in hair of patients with BC was 28.6% lower than the lower limit of the reference values (0.05 μg/g). Decreasing the amount of trace elements in the hair of patients with BC in our view can be explained by the intensive use of its tumor cells, since, according to the A.P. Avtsyn (1991), cobalt has a stimulating effect on cell proliferation to background tissue hypoxia, which is characteristic for tumors [2]. In patients with BC the CI of the content of chromium in hair was within the reference rates.

According to some authors [20, 22], the imbalance of the chemical elements is the basis of the initiation and promotion of cancer pathology, not only through the modulation of metabolism and repair of nuclear and mitochondrial DNA, but also a variety of enzymatic and protein molecules including lysosomal apparatus, immune cells and the activity of antioxidant system. On the other hand, chromium in concentrations causes cell death through activation of apoptotic processes [2].

When determining the content of selenium in the hair of patients with BC it was found that the upper bound of CI concentrations of this microelements was at a level lower limit reference value (0.45 μg/g).

Given the anti-carcinogenic effect of selenium [7] it may be assumed that low levels of the trace element is a risk factor, because the microcell is required to maintain a steady state of cell membranes, suppression of metabolic activation of procarcinogens in a cell, stimulation of reparative DNA synthesis damaged carcinogen, as well as maintain a high antioxidant potential [11].

Multielement analysis of hair of patients with BC showed that the CI content of iodine is in the range of reference values. Iodine — an essential element for the synthesis of thyroid hormones. The action of iodine on the synthesis of these hormones is dependent on the dose. The basis of the effect of increasing doses hormonogenesis on the principle of the two-phase excess iodine — iodine organification increase, and when it reaches a certain critical concentration — unit organification. High doses of iodine inhibits the absorption of iodide, it organification, synthesis and secretion of thyroid hormones, glucose uptake and aminoacids [23, 24]. K.L. Streicher et al. (2004) showed that the level of activity of selenium and selenium-thireoredoxin reductase regulate angiogenesis effect on endothelial growth factor in the breast tumor. In general, a normal iodine balance is closely related with the concentration of selenium and breast diseases [25].

CI of concentrations of manganese and bromine in the hair of patients with BC were in the range of normal values.

Thus, these results indicate that one of important mechanisms of the pathogenesis of BC is the presence of trace elements imbalance in the body of patients. We can assume that in the trace element composition of hair in patients with BC affects developing malignant tumor process associated with the redistribution trace element the pool due to intensive use of them in the metabolism of tumor cells.

CONCLUSIONS

1. Analysis of elements content in hair of patients with BC revealed their trace element status. A reduction of calcium, iron, zinc, copper, cobalt, chromium, selenium rates, and an increase of potassium, sodium, chlorine, and iodine rates were ascertained.

2. Studies have shown the possibility of using the results for the primary prevention and identification of risk groups among women, as well as the usefulness of the correction of specialized treatment medication complexes with trace elements.

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ИЗУЧЕНИЕ МИКРОЭЛЕМЕНТНОГО СТАТУСА БОЛЬНЫХ РАКОМ МОЛОЧНОЙ ЖЕЛЕЗЫ

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Резюме. *Последние 15 лет активно развиваются методики оценки содержания микроэлементов (МЭ) в организме человека по анализу волос. Содержание МЭ в волосах рассматривают в настоящее время как интегральный показатель, характеризующий элементный статус организма.* ***Цель работы:*** *изучение содержания МЭ у больных раком молочной железы (РМЖ) II стадии.* ***Объект и методы:*** *исследованы волосы 30 пациенток с РМЖ II стадии, находившихся на стационарном лечении в Республиканском онкологическом научном центре Министерства здравоохранения Республики Узбекистан в 2016 г. Изучение образцов волос на содержание МЭ (кальций, калий, натрий, хлор, железо, цинк, медь, марганец, кобальт, хром, селен, йод, бром) проводили в лаборатории активационного анализа Института ядерной физики Академии наук Республики Узбекистан инструментальным нейтронно-активационным анализом. Полученные данные о содержании МЭ в волосах пациенток сравнивали с референтными показателями для населения Узбекистана, принятыми в Институте.* ***Результаты:*** *выявлено сниженное содержание железа, цинка, меди, кобальта, и повышенное хлора по сравнению с референтными значениями.* ***Выводы:*** *проведенные исследования указывают на возможность использования данных о содержании МЭ в волосах для первичной профилактики РМЖ и выявления групп риска среди женщин, а также свидетельствуют о целесообразности проведения коррекции специализированного лечения медикаментозными комплексами с добавлением МЭ.*

Ключевые слова: рак молочной железы, микроэлементы, волосы, нейтронно-активационный анализ.

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