THE USE OF HIGH-CURRENT LINAC FOR DETERMINATION THE $^{44}Ca/^{48}Ca$ ISOTOPE RATIO IN CORRELATION WITH ANOTHER ELEMENTS IN DIFFERENT HUMAN PATHOLOGIES

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Chemiluminescence and gamma activation analysis was used to determine the isotopic ratio of calcium in normal, non-malignant and cancerous tissues of thyroid gland. This result was used for diagnostics of cancerous thyroid gland morbidity. The high value of isotopic ratio $^{44}Ca/^{48}Ca$ in paratumor tissues of thyroid gland has allowed concluding about significance of transmembrane circulation calcium.

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INTRODUCTION

The influence of isolated and combined factors of radiation, physical, chemical and biological nature on the human organism promotes occurrence of different anomalies in the organism and, in particular, in the thyroid gland. The pathogeny of the given disease is extremely combined and is investigated insufficiently. Thus the leading role of an autoimmune component is not called in question [1]. Individual features of the person (hormonal, sexual, and emotional) and specificity of metabolic processes proceeding in the human organisms in different ecological regions stipulate the functional activity of thyroid gland. Analysis of available statistical data shows that there is the threshold quantity of atmosphere pollution leading to activation of adaptive potentialities of organism, and, consequently, to reduction of the rate of thyroid gland cancer. The majority of scientific research devoted to diagnostics, search of tumoral markers, problems of treatment and subsequent checking the patients with thyroid gland cancer, includes the whole complex of the tests [2]. However, despite of considerable number of publications, unique answers to many problems till now are not obtained.

The choice of necessary treatment is possible only at valid diagnosis. The majority of research devoted to diagnostics and searching markers of cancerous process and the subsequent control of treatment efficiency is possible with application of the whole complex of examinations. For the last two decades the rate of nodal formations in thyroid gland is observed: for children in tens times, for adults in 3-4 times. There are modern methods (sonoradiography, X-ray computer tomography, nuclearmagnetic resonance tomography, and the radioindicator examinations), giving estimation of available changes. But all of them do not satisfy completely the clinicians. The opportunity of differential diagnostics of malignant and non-malignant process in tissues of thyroid gland is a problem and requires heightened attention to development and upgrading of a system of diagnostics. The facts of calcium level disturbance in blood are known in the case of thyroid pathology [3]. The calcium is universal intermediary during transmit of endocellular signals from the outside and influences on the character of exchange processes. The increase of calcium concentration near the membrane represents a long-term calcium signal, which essentially changes the endocellular control cascade, promotes disturbance of barrier function of membranes for Ca^{2+} ions and can influence on the induction of peroxide oxidation of lipids.

The purpose of the paper is to study the isotopic ratio of calcium and intensity of the free radical peroxide oxidation of lipids in normal, paratumor tissues and malignant tissues of thyroid gland.

METHODS

For measuring the isotopic ratio of calcium the activation analysis by bremsstrahlung radiation from the electron accelerator R&D "Accelerator" was used. After irradiation the isotopic ratio of calcium was measured with a Ge(Li))-detector (volume 50 cm^3, energy resolution 2.2 keV on line 1333 keV). The nuclear reactions $^{48}Ca(\gamma,n)^{47}Ca$, $^{44}Ca(\gamma,p)^{43}K$ induced by a bremsstrahlung radiation and photoneutrons from the electron accelerator with E=25 MeV and current 700 μA were used. The method of chemiluminescence is a direct highly sensitive method for determining electron-excited states of molecular products and gives information about free radical processes [4]. The intensity of chemiluminescence is measured in light quantum's (pulse/s). The volume of the sample measured was 0.2-0.5 ml. Time of measurement was 3-5 minutes. The chemiluminescence measuring of homogenates of tissues, induced with hydrogen dioxide, was conducted on a quantometer with PEA-140. The measurement was conducted in a temperature-controlled bottle at 37°C. The three parameters of luminescence kinetics were analysed: intensity of maximal scintillation (I_{max}), intensity of final value (I_{fin}) and light pulse sum for 4 minutes of measuring (Σ). 28 patients in the age from 12 to 71 years, in total of them 8 men and 20 women were examined. The thyroid gland cancer was detected for 19 patients, for 5 – nodal macrofollicular goitre, for 4 - adenoma of thyroid gland.

The materials were taken from 3 bands: 2 cm^3 of tumor from the tumor centre, 2 cm^3 of tissue on the boundary of tumoral and normal tissue (paratumor) and similar volume of tissue from the non-malignant band. The homogenates of tissues were prepared from 50 mg of tissues examined with the help of mechanical and hand-operated homogenises.

RESULTS

The measuring of the isotopic ratio $^{44}Ca/^{48}Ca$ in tissues of thyroid gland has allowed one to suggest about the transmembrane calcium circulation. The ratios were in normal tissue -1, in paratumor - 1.76, in non-malignant - 0.87, in malignant - 0.58. The error of measurement was 10%. The presented data have shown that the isotopic ratio $^{44}Ca/^{48}Ca$ in cancerous tissues is reduced as compared to normal and paratumor tissues. Probably here the change of

calcium-transporting ability due to transformation of normal tissues into cancerous tissues takes place.

The higher content of the light calcium fraction in paratumor tissue testifies to enhancing its circulation. The disturbance of a membranous Ca^{2+} transport modifies endocellular control cascades, development of membranous damages, which can be the factor of changing the free radical of peroxide oxidation of membrane lipids. It is known that the enhanced circulation of Ca^{2+} is conditioned by the activation of proteinkinase C [5] with phosphorylation of some proteins and realization of long term control stage. On the other hand the activators of a proteinkinase C disturb interlinking with receptors of the cell of tumor necrosis factor (TNF_α) [6]. At the same time the proteinkinase C stimulates production of mRNA coding synthesis of TNF_α. The tumor necrosis factor is executive mediator of inflammation, which causes high values of scintillation chemiluminescence in paratumor. The superexpression of proteinkinase C causes transformation of cells in vitro [6]. In our case the nonreversible activation of proteinkinase C with initiation of cell fission processes is possible [7].

The table represents the data on kinetics of induced chemiluminescence of tissue homogenates.

Table 1.

Form of tissues	I_{max}	I_{fin}
Normal tissues	2060 ± 128	1156 ± 81
Paratumor	6982 ± 111	1877 ± 97
Non-malignanttissues	1231 ± 91	739 ± 39
Cancerous tissues	639 ± 44	392 ± 25

The low intensity of chemiluminescence of malignant tissues is already the proven fact. It is explained by high concentration of inhibitors of free radical of peroxide oxidation**,** which is determined by the high total antioxidative activity of tumor lipids of [8]. The chemiluminescence of paratumor tissue homogenates differ high amplitude of maximal chemiluminescence scintillation that evidences on high oxidizability of lipids in membranes. The sum of chemiluminescence light pulses has high values too. Apparently, the paratumor tissue can be considered as a precursor of cancerous germ formation and consequently of cancerous progression. The intensity of free radical in this case is as inhibitor of cell proliferation. But at the same time higher value I_{fin} evidences that the cancerous progression is caused by accumulation of bioantioxidants. The chemiluminescence method is one of the most sensitive for studying the kinetics of free radical oxidation both in malignant and non-malignant tumors, and in paratumor tissues. The disequilibrium between anti- and proradical products, apparently, is connected with damage of physicochemical properties for membranous calcium transport. Thus, the gamma activation analysis of isotopic ratio of calcium and chemiluminescence methods of estimating free radical oxidation intensity are high-performance research techniques for studying the processes in cancerous and normal tissues of thyroid gland. The character of isotopic ratio between calcium and free radical in tissues of thyroid gland has a definite dependence for normal and malignant processes.

This process can appear to be interdependent cascades in damage of endocellular structures and explains some parties of control in metabolic processes of an organism.

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