Preclinical diagnostics of homeostatic disbalance in plutonium production workers

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Abstract. The purpose of the present is to study the potential of laser correlation spectroscopy of biological samples in preclinical diagnostics of homeostatic disturbances connected with dose loads by internal radiation in plutonium plants personnel. Subfractional composition of expired air condensate, blood serum and urine was examined in 36 males with different doses of internal radiation (between 0.4-130 nCi) by Pu incorporating, and in the control group by the pair choice method. Biological samples were taken in the morning on an empty stomach. A comparative analysis of the results obtained revealed reliable differences in the subfractional composition of the blood serum in somatically healthy volunteers and persons with dose loads. The degree of the revealed homeostatic disturbances raised with increasing the effective dose of internal radiation. Thus, on the basis of the results obtained it can be concluded that only laser correlation spectroscopy of blood serum allows us to estimate the direction and evidence of homeostatic shift in persons exposed to technogenic influence before a detailed clinical picture. Taking into account the dependence of spectral characteristics of biological samples on local peculiarities of population residence, the first reference samples of laser correlative spectrum of blood serum in healthy persons of the Siberian region seem to be the important result of work.

1. Introduction

In the process of arising, developing and functioning industries using nuclear energy different technogenic factors connected with labour or living conditions had an effect on human health. So, of great urgency is the problem of timely diagnostics, treatment and prevention of full value (especially on the individual level) of pathologic states. The influence of the above factors and first of all ionizing radiation (IR) can be the cause of pathologic development. In this connection the problem of studying the individual biological responses of an organism at low-dose radiation effects seems to be one of the most important one in up-to-date radiobiology and radiation medicine.

An effective way to preserve one’s health is considered to be an early revealing of persons in borderline condition (on the verge of the norm and pathology) and preventive measures conducting.

It should be taken into account that at low-dose radiation effects the distant changes in an organism exposed to radiation are developed against the background of a long compensatory tension of its adaptation capabilities caused by the action of radiation and concomitant factors [5]. These changes are realized on all structural and functional levels of an organism and provided with various adaptation mechanisms which in the aggregate are defined as sanogenetic mechanisms. The probability of the onset of a disease in each specific case depends both on the organism resistance and the functional state of systems to be responsible for adaptation as well. So, of paramount importance is an individual evaluation of risk of developing different diseases and intoxications. Taking into consideration the direction of the shift character in biological fluids it is entirely possible to reveal the so-called borderline states, i.e. to judge about reserve opportunities of an organism as a whole. Early identification of homeostatic shift character allows us to select groups of high risk by separate diseases and intoxications and dynamic complex observation of homeostasis can be used as an expertise of the medico-preventive measure efficiency.

One of the most appropriate monitor non-specific methods of laboratory analysis proves to be the method of laser correlation spectroscopy (LCS) that allows us to obtain information on the ratio of hydrodynamic radii of the light-diffusing particles in biological heterogenous fluids quickly and easily [4]. The biophysical LCS essence consists in definition of spectral characteristics of the scattered monochromatic laser radiation by the substrate under study from which by means of mathematical treatment it is possible to restore the histogram of the particle size distribution containing in the fluid examined. In spite of non-specificity of information obtained, the total histogram of the subfractional
composition (HSC) of the fluid studied adequately reflects the ratio of its biosubstrates in the wide range (from 1 nm to 10 µm). No alternative method can allow us to analyze simultaneously the particles having the size from monomer albumins and globular proteins to highly polymerized immune complexes. According to a priori information, in obtaining LCS-spectrum of the blood serum the first light-diffusing zone contains, mainly, low-molecular monomer albumins and glycolipid complexes, the second zone consists of globulins and lipoproteins of high density, the third zone has lipoproteins of low density, the very low-molecular immune complexes, DNA and RNA particles, the fourth zone is filled with immune complexes of medium size and lipoproteins of very low density, the fifth zone reflects immunopoiesis activation with formation of autoimmune complexes but also contains chylomicrons.

Thus, LCS gives a unique opportunity to make not only the structural but also the functional analysis of the corpuscular composition of biological fluids.

Many investigations have shown a principal opportunity of using the method to evaluate the state of anabolic and catabolic processes, immunopoiesis. An increased LCS-sensitivity to form the groups of high risk at oncologic screening of population is demonstrated in literary sources as well [1, 2, 5]. In practice and in experiment it is established that LC-spectra of the blood plasma in patients with precancer states and malignant neoplasms are perfectly differentiated from other somatic diseases of the same localization [1]. The LCS-method is successfully applied in toxicologic examinations, in case of a toxicologo-hygienic expertise and hygienic standardization to define the levels of minimum effective doses (concentrations) of substances tested followed by calculation of safe radiation levels for a man [2, 7].

There is information that LCS makes it possible to evaluate functional tensions in the system of metabolism and humoral immunity occurring at low-dose radiation effects. The problem concerning biological dosimetry of radiation loads by LCS-method is not solved yet. Contradictory literary sources speak for continuation of studying this difficult problem. A wide field of activities to solve these problems is given by the group of SGCE workers and living near-by inhabitants.

2. Material and methods

Examination of the subfractional composition of different biological fluids was made with the aid of a medical device "Spectrometer laser correlation computerized LCS – 03 – "INTOKS". Examination included 36 SGCE workers with different plutonium content in an organism (from 0.4 to 130 nCi) aged 42 – 62 (the mean age 55.6 ± 1.2). The subfractional composition of the blood serum, urine and expired air condensate (EAC) was examined. The metabolism of the radioisotope in an organism was known.

The samples obtained were divided into subgroups depending on the presence – absence of somatic pathology in males examined and in conformity with a dose load. The subgroup C (18 patients) had a small amount of plutonium content (0.4 – 3 nCi), the subgroup D (18 males) had a great amount of plutonium content (10 – 130 nCi). Somatic pathology was observed in 16 patients (subgroup A) including hypertension in 10 patients, out of them, 6 males had ischemic heart disease. Chronic bronchitis was diagnosed in 8 men. The other 20 males (subgroup B) were practically healthy.

The so-called total spectrum was analyzed to study HSC applying to one ground under examination. It was obtained as a result of arithmetical averaging of standard individual HSC and it allowed us to judge about the most characteristic type of the particle distribution function by hydrodynamic dimensions and contribution to light diffusion for the aggregate studied. It is assumed to single out discrete differentially significant zones (by light-diffusing particle sizes) to obtain an objective characteristic of homeostatic shift variants by abscissa axis [4]. There are the following zones for blood plasma: from 0 to 10 nm (zone 1), from 11 to 30 nm (zone 2), from 31 to 70 nm (zone 3), from 71 to 150 nm (dimensions of light-diffusing particles). For urine they are from 0 to 10 nm (zone 1), from 11 to 55 nm (zone 2), from 56 to 250 nm (zone 3), from 250 to 1000 nm (zone 4), more than
1000 nm (zone 5). These recommendations were taken into account when analyzing the group LC-spectra of all biological fluids obtained.

3. Results and discussion

The examples of the obtained spectra of the blood serum, urine and EAC are given in Fig. 1.

It is clearly seen from Fig. 1 that the main characteristic of LC-spectrum of blood plasma seems to be bimodality of the particle distribution histogram with great contribution to light diffusion of particles with an average hydrodynamic radius of 80-600 nm, i.e. monochromatic laser radiation is scattered, mainly, on medium- and large-molecular globulins of blood plasma. For histogram of the subfractional urine composition, the appearance of particles having large hydrodynamic radii in keeping spectrum bimodality in the same range seems to be a typical feature. EAC has rather poor corpuscular composition by the norm showing, on the whole, the character of particle distribution of the above biological fluids.

The percentage distribution of contribution to light diffusion according to the above 5 zones (fractions) was studied to analyze intergroup differences of the subfractional composition of biological media examined.
Correlation of the subfractional composition of the blood serum, urine and EAC revealed clearly marked differences of biosubstrates analyzed in males with somatic pathology (subgroup A) as compared with practically healthy persons (subgroup B) that is shown in Fig. 2-4.

Note: at this point and that one in Figures K is a hydrodynamic radius of particles in nm.

FIG. 2. Subfractional evaluation of contribution of biosubstrate EAC by LCS method in subgroups A (1) and B (2).

FIG. 3. Subfractional evaluation of contribution of biosubstrate urine particles by LCS method in subgroups A (1) and B (2).
Less expressed differences were observed in the subfractional urine composition in the subgroups compared. Group spectra demonstrated a comparable level of microalbuminuria. Persons with somatic pathology had only an increase of contribution to light diffusion of fraction 5 containing large-molecular albuminoimmune complexes connected with immunopoiesis activation.

The comparative analysis in subgroups with different radiation load (C, D) was carried out to verify the contribution of the radiation component to homeostatic disturbance list formation among workers of the main production.

The subfractional urine composition in persons with different dose load was of no statistical significance. One can note only indistinct tendency to a contribution decrease of fraction №4 by rising fraction №5.

The present research has shown only negligible tendency to the prevalence of small particles in EAC in patients with a large plutonium content that reflects an increase of eliminating toxins with the expired air and more intense functioning of the respiratory system. A contribution decrease to light diffusion of particles with medium-size hydrodynamic radius is combined with compensatory increase of fraction 5 showing modification of the immune response on the level of alveoli connected, probably, with inhalation way of radionuclide entering the production.

The most impressive differences are obtained when comparing the corpuscular composition of the blood serum in the subgroups examined (Fig.5). A decrease of contribution to light diffusion of small particles (zone 1, 2) characterizing inhibition of catabolic processes at sufficient functional tension of excretory systems is noted in the subgroup D. Of great interest is the tendency to increasing fractions 3 and 4 with decreasing contribution of particles forming zone 5. These shifts of varied direction, probably, reflect clearly marked immune response in patients with a small dose load and adaptation failure, compensatory adaptive mechanisms breakdown in persons with a large radiation dose.
FIG. 5. Subfractional evaluation of contribution of biosubstrate particles of the blood serum to light diffusion by LCS method in subgroups D (1) and C (2)

4. Conclusion

1. The LCS-method allows us to study the subfractional composition of different biological media (EAC, urine, the blood serum or plasma serum), verify the directivity and manifestation degree of metabolic shifts in patients without somatic pathology exposed to technogenic effects.
2. LCS of biological fluids gives an opportunity to record changes (disturbances) in the main homeostatic links accompanying the course of different somatic diseases (even beyond an acute attack of a disease) or being pathogenetic links defining regularities of the given nosologies development.

3. LC-spectroscopy of the blood serum is of great informativity for diagnostics of preclinical homeostatic disturbances.

Reference: