Study of the penetrating ability of 5% glucose solution into insulin-dependent cells of mouse organs, under the influence of ionising radiation

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Abstract. The aim of the work is to study the penetrating ability of a 5% glucose solution into damaged insulin-dependent tissues of the body, under the influence of various doses of ionising radiation. Hypothesis. Since there is a certain level of glucose in the blood, it is possible to assume increased damage to cells under the influence of an excessive amount of glucose penetrating into cells not only with the help of carrier proteins, but also through radiation-damaged cell membranes. Materials and methods. In order to assess the damaging effect of ionising radiation, insulin-dependent organs were used. The animals were divided into 3 groups. The first group consisted of organs of 10 mice that received a dose of ionising radiation of 1 g. The second group consisted of organs of 10 mice that received a dose of ionising radiation of 2 Gy. The third group consisted of the organs of 10 mice that received a dose of 3GH ionising radiation. Results and discussion. Depending on the dose of irradiation of organ groups, we found a direct dependence of the decrease in the content of residual glucose in the nutrient medium 6 hours after irradiation. And inversely proportional dependence of glucose content 24 hours after irradiation. The strongest penetrating power of 5% glucose is observed when irradiated with a radiation dose of 2 Gy. Under the influence of ionising radiation, target cells were stained more intensively with hematoxylin-eosin than intact tissues, regardless of the radiation dose. Conclusions. Therefore, the in vitro study reflects both changes in residual glucose level in the nutrient medium, without active participation of glucose and insulin carrier proteins, and intracellular changes under the influence of ionising radiation damaging factors on animal organ cells.

1 Introduction

The uptake of glucose from the environment by the bulk of cells, except brain cells and erythrocytes [1, 2, 4] occurs under the influence of insulin and intracellular carrier proteins (GLUT 1, GLUT 2, GLUT 3, the others work in enterocytes and liver cells against the

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concentration gradient) [6]. These transporter proteins work at the level of the two layers of the lipid membrane of insulin-dependent cells.

The objective is to study the penetration capacity of 5% glucose solution into damaged insulin-dependent tissues of the body under different doses of ionising radiation.

The hypothesis is as follows: one of the consequences of radiation exposure is oxidative degradation of lipid layers of cell membrane by free radicals (FRO) [7]. Since a certain level of glucose is present in the blood, an increase of cell damage by excess glucose entering the cells can be assumed not only by means of carrier proteins, but also through radiation damaged cell membranes. Since the complete oxidation of 1 mol of glucose allows the synthesis of up to 38 mol of ATP during aerobic glycolysis and 2 mol of ATP during anaerobic glycolysis, the transition of damaged cells to anaerobic glycolysis [3, 5, 8] may be supposed to be a protective cellular reaction against glycosylation by excess glucose intracellular structures.

2 Materials and methods

The study was carried out at the clinical site of the BSMU Department of Oncology with courses in oncology and pathological anatomy with courses in IDPO. To study the results of the application of ionising radiation, 30 BALB / c mice with intact different sex, 15 samples of each sex, were included in the study. The animals were aged from 2 to 3 months. Body weight was 18 to 22 grams. The insulin dependent organs, such as kidneys, spleen, lungs and heart, were used to evaluate the damaging effects of ionising radiation. Animals were slaughtered under the influence of ether vapours, 10 minutes after the onset of anaesthesia. Organs were washed with blood in 0.9% NaCl solution. The animals were divided into 3 groups. The first group consisted of the organs of 10 mice which received 1 Gy dose of ionising radiation. The second group consisted of 10 mice with 2 Gy dose. The third group comprised organs of 10 mice exposed to 3 Gy ionising radiation respectively. For comparison, organs from intact mice were used as controls. A 5% -5.0 ml glucose solution was used as nutrient medium for the organs of each group. For histological examination, the same animal organs damaged and undamaged by ionising radiation were taken. After appropriate histological preparation and preparation of 7 µm thick sections, the sections were stained with hematoxylin-eosin. A total of 75 micropreparations were prepared.

3 Results and discussion

Depending on the dose of organ group irradiation we found a direct correlation between the decrease in residual glucose content in the nutrient medium at 6 hours after irradiation. And an inversely proportional relationship of glucose content 24 hours after irradiation (Table 1).

Considering the histological preparations, we found more intensive haematoxylin-eosin staining in all groups of irradiated organs compared to controls (Fig.1).



Fig. 1. On the left are intact lungs. On the right, lungs irradiated with 1 Gy.

Hematoxylin-eosin staining, x100

 Table 1. Changes in glucose values in 5% glucose solution as a function of radiation dose and time after exposure

Time after exposure	Balb/c animal groups	Glucose level in the nutrient medium (mmol/l)														Correla tion linkage	
		Radiation dose 1 Gy.					Radiation dose 2 Gy.					Radiation dose 3 Gy.					
6 hours	test	35	25	25	30	50	40	20	25	25	25	50	45	35	30	30	p<0.05
	control	50	50.5	45	40	70	45	50	45	40	70	135	55	40	40	35	p<0.05
24 hours	test	55.5	60	50	45	40	40	45	65	55.5	50	55.5	50	40	50	55	p<0.05
	control	55.5	55	45.5	40	45	35.5	45.5	60.5	55.5	50.5	55.5	55	40	45	60	p>0.05

In animals irradiated with -1 Gy dose the lung histostructure has a number of changes. It concerns disturbances of blood circulation, manifested in the form of venous hyperemia. The lumen of alveoli shows inflammatory phenomena (Fig. 1). At the same time, lung alveolocytes do not undergo destructive changes, the structure of both secretory and respiratory ones is also not changed.

Animals irradiated with -1 Gy have a number of changes in the histostructure of the kidney. This concerns circulatory disturbances manifested by venous hyperemia. The lumen of individual tubules or a group of tubules contains cylinders of protein-carbohydrate nature, in the area of cylinders location the tubule lumen is dilated (Fig.2) At the same time, epithelial cells of renal tubules do not undergo destructive changes, the structure of basal membrane of epitheliocytes is also not changed.



Fig. 2. On the left is the intact kidney. On the right, the kidney irradiated with 1 Gy. Severe venous hyperemia and protein-carbohydrate components (cylinders) in the renal tubules of animals irradiated with 1 Gy. Hematoxylin-eosin staining, x100



Fig. 3. On the left is the intact spleen. On the right, the spleen irradiated with 1 Gy. Hematoxylin-eosin staining, x100

Animals irradiated with -1 Gy in the spleen also show an irregular histostructure, i.e. weak in the white pulp and moderate reaction in the red pulp, with more intensive staining with haematoxylin-eosin (Fig. 3).



Fig. 4. On the left are intact lungs. On the right, lungs irradiated with 2 Gy.

Hematoxylin-eosin staining, x100

In animals irradiated with 2 Gy the lung histostructure has the same number of changes as in the organs of animals irradiated with 1 Gy. It concerns circulatory disturbances manifested by venous hyperemia. In the lumen of alveoli there are phenomena of inflammatory nature (Fig.4). More saturated staining with haematoxylin-eosin compared to the control group. Lung alveolocytes do not undergo destructive changes, the structure of secretory and respiratory alveolocytes is also not changed.



Fig. 5. On the left is the intact kidney. On the right, the kidney irradiated with a dose of 2 Gy.

Hematoxylin-eosin staining, x100

Animals irradiated with -2 Gy have a number of changes in renal histostructure similar to those in animals irradiated with 1 Gy. This refers to circulatory disturbances manifested as venous hyperemia (Fig.5). At the same time, epithelial cells of renal tubules do not undergo destructive changes, the structure of basal membrane of epitheliocytes is not changed.



Fig. 6. On the left is the intact spleen. On the right, the spleen irradiated with a dose of 2 Gy. Hematoxylin-eosin staining, x100

For animals irradiated with -2 Gy dose in the spleen the histostructure is also irregular as in the groups irradiated with 1 Gy dose, i.e., weak reaction in the white pulp and moderate reaction in the red pulp, more intensive staining with haematoxylin-eosin is observed (Figure 6).



Fig. 7. On the left, intact heart muscle tissue. On the right, cardiac muscle tissue irradiated with a dose of 2 Gy. Hematoxylin-eosin staining, x200

Animals irradiated with 2 g dose showed the same increase of intensity of hematoxylineosin staining of cardiomyocytes as in the group of animals irradiated with 1 g dose. No pronounced destructive changes in cardiac muscle cells were detected (Fig.7).



Fig. 8. On the left are intact lungs. On the right, lungs irradiated with 3 Gy. Hematoxylin-eosin staining, x100

Animals irradiated with 3 Gy have the same lung histostructure as the organs of animals irradiated with 1 and 2 Gy respectively. This also concerns bleeding disorders manifested by venous hyperemia and diapedesis of hemorrhages into surrounding tissues. The lumen of the alveoli shows inflammatory phenomena (Fig. 8). More saturated staining with haematoxylineosin compared to the control group. Lung alveolocytes do not undergo destructive changes, the structure of secretory and respiratory alveolocytes is also unchanged.



Fig. 9. On the left is the intact kidney. On the right, the kidney irradiated with 3 Gy.

Hematoxylin-eosin staining, x100

Animals irradiated with -3 Gy have the same kidney histostructure as animals irradiated with 1 and 2 Gy. respectively. This refers to circulatory disturbances manifested as venous hyperemia (Fig.9). At the same time, epithelial cells of renal tubules do not undergo destructive changes, the structure of basal membrane of epitheliocytes is not changed.



Fig. 10. Intact spleen. Right spleen irradiated with 3 Gy.

Hematoxylin-eosin staining, x100

Animals irradiated with dose of -3 Gy in the spleen also show uneven histostructure similar to the groups irradiated with dose of 1 and 2 Gy, i.e., weak reaction in the white pulp, moderate reaction in the red pulp, more intensive staining with haematoxylin-eosin (Fig.10).



Fig. 11. On the left is intact heart muscle tissue. On the right, cardiac muscle tissue irradiated with 3 Gy. Hematoxylin-eosin staining, x10

Animals irradiated with the dose of 3 g have also increased intensity of staining of cardiomyocytes with hematoxylin-eosin as in the group of animals irradiated with the dose of 1 and 2 Gy respectively. There is a loosening of muscle fibers. No pronounced destructive changes in the heart muscle cells themselves were detected (Fig.11).

4 Conclusions

- 1. Depending on the dose of organ group irradiation, we found a direct correlation between the decrease in residual glucose content in the nutrient medium 6 hours after irradiation. And inversely correlated to the glucose content 24 hours after irradiation
- 2. The strongest permeability of 5% glucose was observed with a radiation dose of 2 Gy.
- 3. Under ionising radiation, the target cells stained more intensively with hematoxylin-eosin than the intact tissue, irrespective of radiation dose.

5 Summary

Thus, the In vitro study reflects both the change in the level of residual glucose in the nutrient medium, without active participation of glucose transporter proteins and insulin, and intracellular changes under the influence of damaging factors of ionising radiation on animal organ cells.

These processes in tissues can also be correlated with processes occurring in the macroorganism, where there is always a certain level of glucose and any other damaging factors occurring in everyday life, such as biological (viruses, bacteria), chemical, thermal, etc. This mechanism of damaging effects of excess glucose can be a trigger in carcinogenesis.

A growing number of studies are proving the link between diabetes mellitus and cancer. Diabetic patients are at increased risk of developing several types of cancer. The strongest association is between diabetes mellitus and pancreatic and liver cancer, and diabetic patients have an increased risk of breast, uterine, bladder, and kidney cancer. Insulin resistance and hyperinsulinemia, chronic systemic inflammation and hyperglycaemia are the pathophysiological basis of the relationship between diabetes and cancer. Insulin is a growth factor that promotes cell proliferation. The mitogenic effect of hyperinsulinemia is more pronounced in malignant cells, which often overexpress insulin receptors. Hyperglycaemia provides energy for malignant cell proliferation and promotes cancer growth and neoangiogenesis [5].

Conflict of interests. The authors state that they have no conflict of interests.

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