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ASSESSMENT OF MEDICAL EXPOSURE IN PALLIATIVE THERAPY WITH SAMARIUM – 153

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ABSTRACT

The scientific article is devoted to an actual problem - medical exposure. **The aim** of the study is to assessment the doses of irradiation of organs and tissues during palliative treatment patients with metastasized bone cancer. Over the past 20 years, only samarium-153 has been used for these purposes in Uzbekistan. **Materials and methods.** For the study, data from radioisotope laboratories of Tashkent medical institutions, where palliative treatment is carried out, were used. Radionuclide therapy with samarium-153, oxabiphor, was performed on 78 women who were diagnosed with mammary cancer, who had multiple bone metastases and pain syndrome. Equivalent doses of irradiation of the organs of patients were calculated by multiplying the introduced activity in MBq by the dose coefficients of the absorbed dose in mGy for specific organs per 1 MBq of activity. **Results.** Depending on the weight of the patients, dose loads on the bladder were in the range of 1.2–2.0 Gy; liver - 0.01 -0.02 Gy; kidneys - 0.6 - 1.0 Gy; small intestine - 0.01 - 0.02 Gy; the lower part of the large intestine - 0.02 - 0.03 Gy; upper colon - 0.01 - 0.02 Gy; ovaries - 0.02 - 0.03 Gy; whole body - 0.2 - 0.03 Gy. **Conclusion.** Due to the selective accumulation and manifestation of deterministic effects in the bone tissue, a decrease in pain in patients with metastasized bone lesions is clearly expressed. Equivalent radiation doses to other organs are below critical levels, so the risk of deterministic damage is minimal. The bladder experiences the greatest dose loads, then the kidneys, the lower part of the large intestine, the ovaries, small intestine, and the upper colon.

Key words: radionuclide medicine, samarium-153, oxabiphor, equivalent dose of radiation, palliative therapy, radiopharmaceutical.

INTRODUCTION

According to the World Health Organization, 19.3 million people fell ill with cancer in the world in 2020, 10 million people died as a result of this disease. The situation became more complicated due to the COVID-19 pandemic, when health systems were working at the limit of their capabilities and all resources were directed to the fight against coronavirus [1].

In the structure of the incidence of malignant neoplasms (MN) for 2021, breast, stomach and cervical cancers retain leading positions with incidence rates of 9.8; 5.1; and 4.8 per 100 000 population, respectively. The structure of oncological morbidity among the female population is as follows: breast MN - 19.5; cervical MN - 9.7 and ovarian MN - 4.9 per 100,000 population, and among the male population: stomach MN - 6.2; bronchial and lung MN - 5.4 and prostate MN - 3.0 per 100,000 population [2].

Metastatic bone damage is one of the most common complications of solid cancer. According to the literature, the frequency of such lesions of the bone system in breast cancer at different stages of the disease is 47-85%, prostate cancer — 33-85%, lung cancer — 30-60%, kidney — 33-40%, thyroid cancer — 28-60% [3,4]. At the initial stages, metastatic bone damage is often clinically asymptomatic, but later manifests itself as malignant hyperkalemia, fractures and pain syndrome, which significantly reduces the quality of life of patients [5].

Radionuclide therapy of multiple metastatic skeletal lesions has been widely used in the world since the late 80s of the last century [6,7,8]. The greatest experience of the successful use of radionuclides in palliative therapy has been accumulated in prostate cancer and BPH, which is explained by the nature of the lesion of the bone system (the presence of a pronounced blast component) [9]. In world practice, isotopes 32P, 89Sr, 186Re, 188Re, 153Sm and 177Lu are actively used for palliative therapy of bone metastases [10]. The use of radionuclide therapy for the treatment of bone metastases is due to the ability of some beta-emitting isotopes to selectively accumulate in pathological foci with increased mineralization and increased metabolism of bone tissue. Local "internal" irradiation with β-particles equally affects both the manifesting and subclinical foci of bone destruction, which makes it possible to achieve reduction of tumor infiltration and provide anesthesia [11,12].

The formation of maximum doses of the drug in the most functionally active metastases provides a basis for achieving rapid and effective suppression of pain syndrome [13].

Due to the presence of gamma quanta in the 153Sm radiation spectrum, the scintigraphic picture obtained with any labeled phosphate compound before treatment is completely comparable to the distribution of the radiopharmaceutical (RFP) in the bones after its administration.

According to the literature, 153Sm is characterized by a rapid response to the introduced activity, which is its distinctive feature compared to phosphorus and strontium. On average, the effect of the therapy occurs 2-7 days after the introduction of RPF and lasts an average of 4-12 weeks [14]. The overall clinical efficacy of samarium-153 therapy depends on the primary localization of the tumor process. Evaluation of the results of repeated injections showed that therapy carried out after 3 and 6 months is also effective.

Work with the drug should be carried out in accordance with SanPiN No. 0193-06 "Radiation safety standards (NRB-2006) and basic sanitary rules for radiation safety (OSPORB-2006)".

The aim of the study was to evaluate the doses of irradiation of organs and tissues during palliative therapy with Samarium in 153 patients with metastasized bone cancer.

Materials and research methods. For the last 20 years in Uzbekistan, only Samarium-153 has been used for palliative treatment of metastasized bone cancer.

Samarium-oxabiphor, 153Sm is a colorless transparent solution for intravenous administration. The 153Sm isotope emits beta radiation with an energy of 640 keV, 710 keV, 810 keV with yields of 30%, 50% and 20%, respectively, and gamma rays with an energy of 103 keV. Half-life of 153Sm - 46.2 h.

For the study, data from radioisotope laboratories of medical institutions in Tashkent were used, in which palliative therapy of patients with metastatic bone cancer with Samarium-153 oxabiphor is carried out. Radionuclide therapy with samarium-oxabiphor, 153Sm was carried out in 78 breast cancer patients with multiple bone metastases and pain syndrome. The age of the patients ranged from 28 to 70 years (mean 48.7 years). The duration of the disease before the start of radionuclide therapy ranged from 6 to 240 months. (average 61.5 months). Of the 78 patients, bone metastases were already present in 10 women when the disease was detected, in 68 they appeared after the diagnosis was established. All patients previously received various treatment: hormone therapy, radiation, chemotherapy, surgical treatment. Samarium-oxabiphor, 153Sm was injected intravenously. Women who first came to receive palliative care were selected. In Uzbekistan, for palliative therapy of bone cancer, samarium-153 oxabiphor is administered to patients at the rate of 1 mCi of activity per 1 kg of the patient's weight, 1 mCi is equal to 37 MBq. This treatment is carried out only in patients over 18 years of age.

Table 1 shows the distribution of patients by body weight in the range of 5 kg.

Table 1

Distribution of patients with metastasized bone cancer participating in the study, by body weight

Number of patients	**Weight of patients, kg**						
	45-50	**51-55**	**56-60**	**61-65**	**66-70**	**71-75**	**76-80**
78	5	19	21	18	8	6	1

The effectiveness of treatment was assessed by the dynamics of the pain syndrome for 3 months after drug injection. For this, a 10-point visual analogue scale was used (0 points - no pain, 10 points - the most severe pain). The effect was self-assessed by the patient one, two and three months after the injection.

The dynamics of the "quality of life" was determined according to the Karnovsky scale, according to which the patient's activity is assessed: 0-40% - unable to serve himself, hospital care is required, rapid progression of the disease is possible; 50-70% - loss of ability to work, living at home is possible, for the most part is able to serve himself, care is required in a different amount; 80-100% - normal daily activity is preserved, medical care is not required [15].

Equivalent doses of irradiation of the organs of patients were calculated by multiplying the introduced activity in MBq by the dose coefficients of the absorbed dose in mGy for individual organs per 1 MBq of activity.

With intravenous administration of the solution, there is a high and selective accumulation of Samarium - 153 oxabiphor in metastatic organs and rapid excretion from healthy tissues. A preliminary assessment of the accumulation of radiopharmaceuticals can be carried out, if necessary, using bone scintigraphy with technefor or pyrfotech preparations containing radioactive technetium-99. According to the officially approved instructions for use of the drug, compiled on the basis of the electronic edition of the Vidal 2014 guide, updated on December 7, 2019, the absorbed doses of various organs in mGy per 1 MBq of the administered activity of Samarium-153 oxabiphor were determined, which amounted to - 0.702 mGy/MBq, liver - 0.0067, kidneys - 0.351, small intestine - 0.00783, lower large intestine - 0.00999, upper large intestine - 0.0051, testicles - 0.00756, ovaries - 0, 00918. For the whole body, the coefficient for determining the effective equivalent dose is 0.01161 mSv/MBq. In the palliative treatment of metastatic bone cancer, determining the effective dose is not so important, because the concept of effective dose was introduced to assess the long-term effects of human exposure to low doses. Small doses mean that they cannot have deterministic effects, i.e. cause radiation damage to any tissue. The goal of radionuclide therapy (RNT) is the opposite - to cause the death of tumor tissue, therefore, radiation exposure in RNT is described by equivalent doses in individual organs and target tissues.

For statistical data processing, the main methods of descriptive statistics were used: measures of central tendency and measures of variability. From the measures of the central tendency, the arithmetic mean was determined, from the measures of variability, the standard deviation.

Distributions (samples) were checked for normality using the Kolmagorov-Smirnov test. Significant differences between the samples were determined using the Mann-Whitney U-test. Statistical analysis was carried out using statistical programs OriginPro 8.6, SPSS Statistics 17.

Results and discussion. After intravenous administration, the drug selectively accumulated in the skeletal system, mainly in foci with increased mineral metabolism (metastases). The presence of gamma radiation (103 keV) in 153Sm made it possible to obtain a scintigraphic image on gamma cameras.

The decrease in pain intensity began to appear in most cases (in 48 of 78 patients - 61.5%) in the interval from one to two weeks after the injection. In 19 (24.3%) patients, pain began to decrease earlier than this period, and in 11 (14.2%) patients, later. It was difficult to accurately determine the day of onset of anesthesia due to the gradual manifestation of the clinical effect. The dynamics of the pain syndrome looked like this on a 10-point visual analogue scale. At the beginning of therapy, the average figures for the intensity of bone pain were 6.5 points, after 2 weeks and within 3 months, the pain was, according to a 10-point scale, at the level of 3.2 + 0.3 points. The minimum average pain intensity score was 2.41 points. The data is presented in Figure 1.

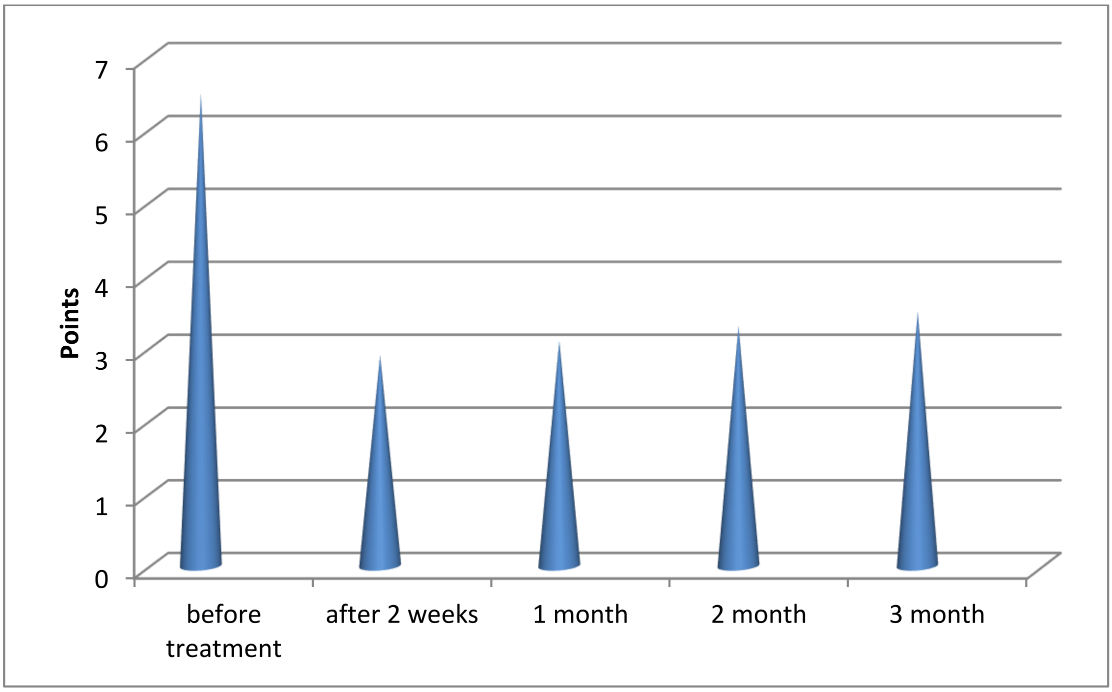

Fig. 1. Dynamics of average values of pain syndrome in patients with breast cancer with bone metastases after therapy with samarium-oxabiphor, 153Sm, according to the visual analogue scale of pain from 0 to 10 points

Before the start of treatment, in most of the observed female patients, the "quality of life" according to the Karnovsky scale was at the level of 55-60%, after 2 weeks and within 3 months - at the level of 70 + 5%. The data is shown in Figure 2.

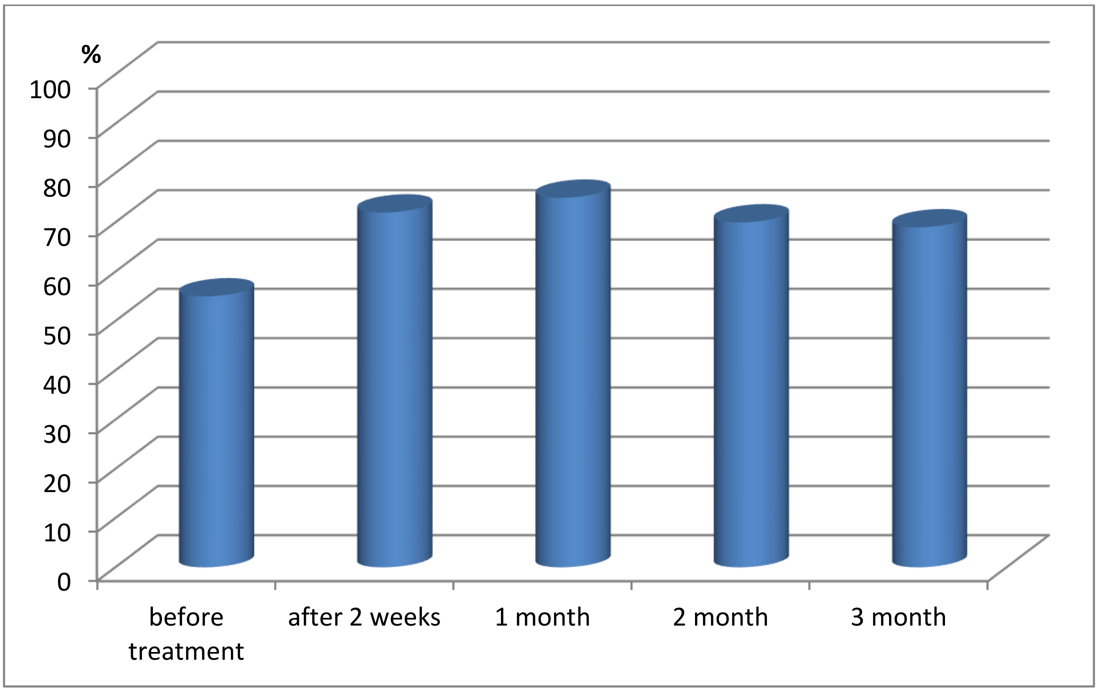

Fig.2. Dynamics of "quality of life" in patients with breast cancer with bone metastases after the therapy with samarium - oxabiphor, 153Sm, based on the Karnovsky scale in the range of 0-100%

Based on the introduced activities per 1 kg of body weight of patients, the equivalent doses of organ irradiation were determined. The average and total values of the activities administered to patients, depending on the weight and number of patients, are presented in Table 2.

Table 2

Average values of the obtained radiopharmaceutical activity by pations with metastasized bone cancer depending on the patient's body weight

Weight of patients, kg	**Number of patients**	Total injected activity, MBq	Average values of injected activity, MBq
45-50	5	8806,9	1761,20 ± 47,36
51-55	19	36630,5	1952,66 ± 50,22
56-60	21	45695,7	2175,71 ± 198,16
61-65	18	42294,1	2314,41 ± 43,80
66-70	7	18093,8	2504,22 ± 44,33
71-75	5	13651,2	2693,07 ± 40,77
76-80	3	8875,1	2904,50 ± 18,50
45-80	78	174047,3	2231,38 ± 264,87

Table 3 shows the calculated equivalent doses of irradiation of organs and tissues during palliative treatment with Samarium-153 oxabifor.

Table 3

The results of determining the equivalent doses of irradiation of organs and tissues during radionuclide therapy with Samarium-153

Organs	Equivalent doses, mGy						
	Weight of patients, kg						
	45-50	51-55	56-60	61-65	66-70	71-75	76-80
bladder	1236,4 ± 33,2	1370,8± 35,3	1527,4± 139,1	1624,7± 30,7	1757,9± 31,1	1890,5± 28,6	2038,9± 12,9
liver	11,80 ± 0,31	13,08 ± 0,33	14,58 ± 1,32	15,50 ± 0,29	16,77 ± 0,29	18,04 ± 0,27	19,46 ± 0,12
kidneys	618,2 ± 16,6	685,4 ± 17,6	763,7± 69,6	812,3± 15,3	878,9± 15,5	945,3± 14,3	1019,4± 6,5
small intestine	13,8 ± 0,4	15,3 ± 0,4	17,0 ± 1,5	18,1 ± 0,3	19,6 ± 0,3	21,1 ± 0,3	22,7 ± 0,1
lower part of the colon	17,6 ± 0,5	19,5 ± 0,5	21,7 ± 1,9	23,1 ± 0,4	25,0 ± 0,4	26,9 ± 0,4	29,0 ± 0,2
upper part of the colon	8,9 ± 0,2	9,9 ± 0,3	11,1 ± 1,0	11,8 ± 0,2	12,8 ± 0,2	13,7 ± 0,2	14,8 ± 0,1
ovaries	16,4 ± 0,3	17,9 ± 0,4	19,9± 1,6	21,3 ± 0,4	23,0 ± 0,4	24,7 ± 0,4	26,7± 0,2
whole body	20,4 ± 0,5	22,7 ± 0,6	25,3 ± 2,3	26,9 ± 0,50	29,1 ± 0,5	31,3 ± 0,5	33,7 ± 0,2

From the obtained results of the study, it can be seen that in the case of palliative treatment with Samarium-153, in addition to the selective accumulation of radiopharmaceuticals in metastatic and inflammatory-destructive foci of bone tissue, the bladder experiences a large dose load, then the kidneys, the lower part of the large intestine, ovaries, small intestine, upper section of the large intestine. These data are shown in Figures 3-5.

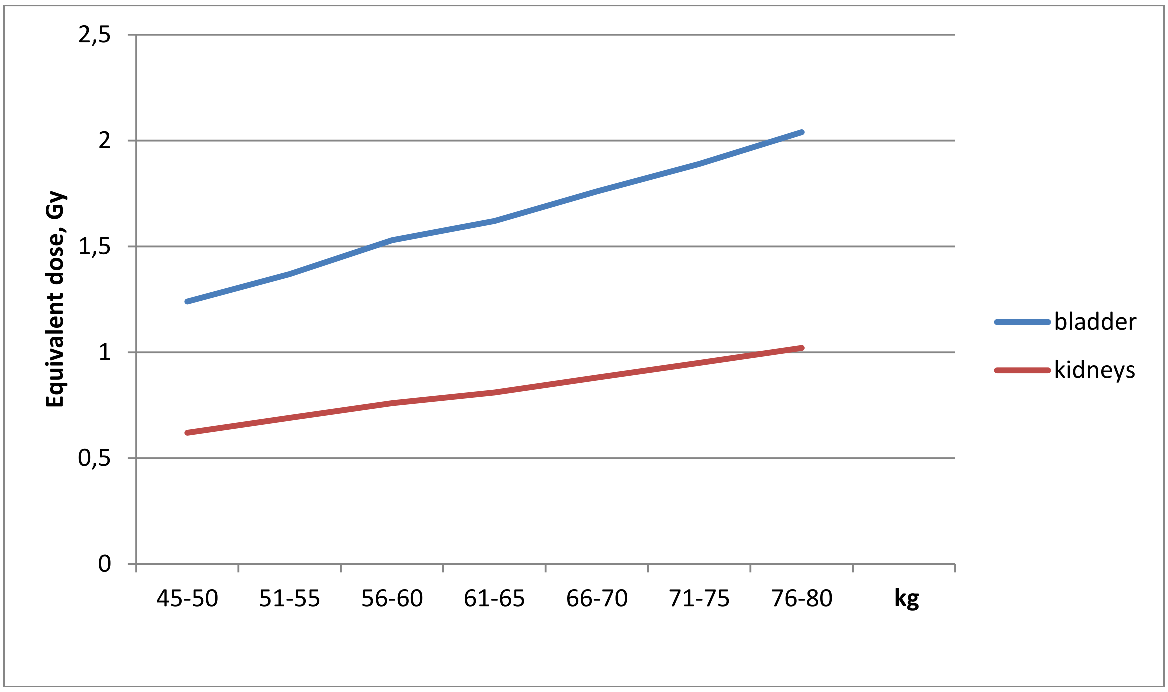

Fig.3. Dynamics of values of equivalent doses of irradiation of the bladder, kidneys, depending on body weight of patients

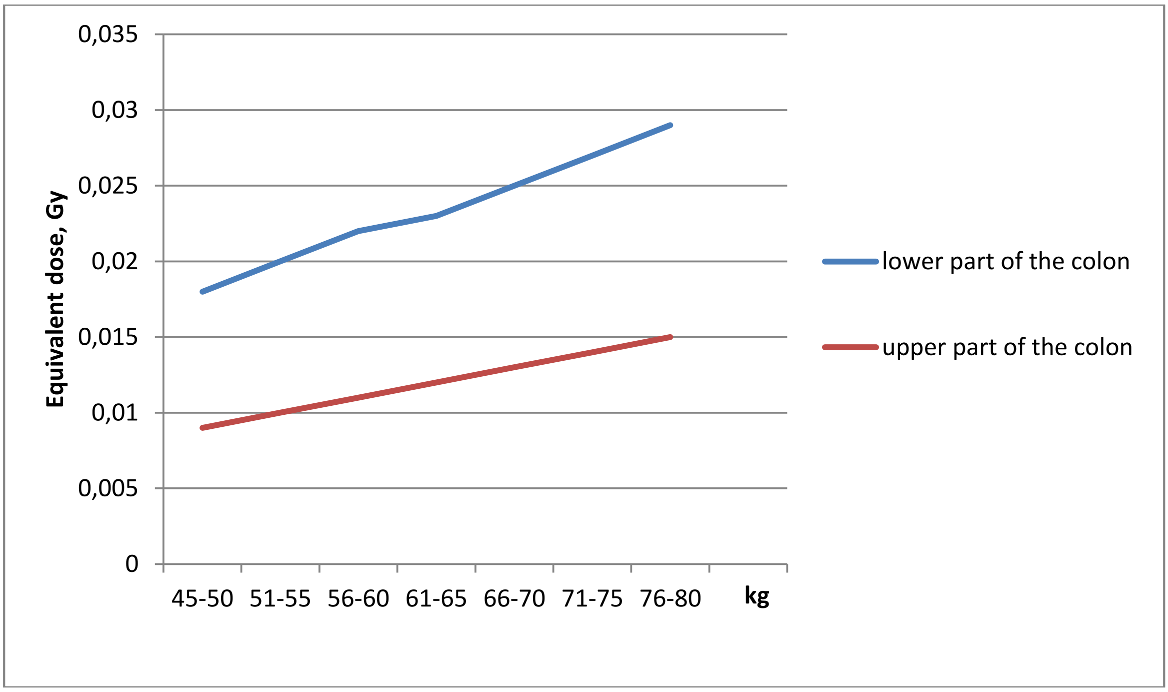

Fig.4. Dynamics of the values of equivalent doses of irradiation of the lower and upper parts of the colon, depending on body weight of patients

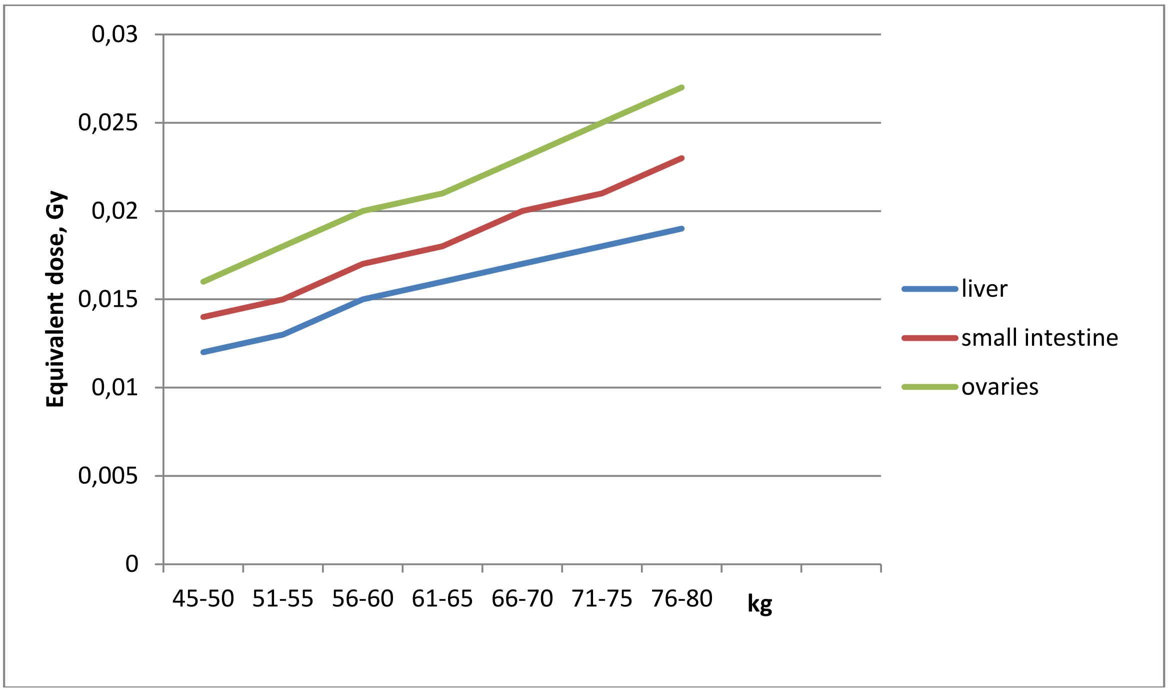

Fig.5. Equivalent of values doses dynamics of irradiation of the liver, small intestine, ovaries depending on body weight of patients

The equivalent dose to the whole body is in the range of 20.44 - 33.72 mSv. All received equivalent doses are below the dose thresholds required to produce deterministic effects.

The advantages of Samarium-153 oxabiphor are rapid excretion from healthy tissues, relatively low toxicity of the drug, and a good analgesic effect.

Conclusion.

The results of the conducted studies prove that despite the irradiation of all organs and tissues during radionuclide therapy with Samarium-153, the benefits of this procedure are greater than the harm. Due to the selective accumulation and manifestation of deterministic effects in the bone tissue, a decrease in pain in patients with metastasized bone lesions is clearly expressed. Equivalent radiation doses to other organs are below critical levels, so the risk of deterministic damage is minimal. The greatest dose load is experienced by the bladder, then the kidneys, the lower part of the large intestine, the ovaries, the small intestine, and the upper part of the large intestine.

The use of radionuclide therapy in the complex treatment of metastatic lesions of the skeletal system in malignant tumors of various localization confirms the need for greater introduction into medical practice, the development of new radiopharmaceuticals that have a high specificity of accumulation in the focus, a pronounced analgesic effect with minimal side effects.

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