KINETICS OF ^{153}Sm OXABIPHOR IN THE BLOOD OF CANCER PATIENTS UNDERGOING COMPLEX THERAPY FOR BONE METASTASIS

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Concentration ^{153}Sm in the blood of patients with bone metastasis after radionuclide therapy was determined. Considerable variation of the content of ^{153}Sm in blood of patients with various primary cancers from 10 to 65 Bq/ml is found. The effective half-life of ^{153}Sm in the blood of patients was estimated at more than 10 days during the course of the therapy.

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1. INTRODUCTION

^{153}Sm oxabiphor is a major therapeutic agent that is widely used for effective palliative treatment of skeletal metastases from various primary cancers [1,2]. This radiotracer has excellent analgesic properties and minimum side effects.

The radioactive isotopes ^{32}P, ^{89}Sr, ^{90}Y, ^{186}Re and ^{153}Sm etc. are used in radionuclide therapy for the treatment of widespread bone metastases [3].

Three radioisotopes are currently approved for the treatment of bone pain: phosphorus-32 (^{32}P), strontium-89 (^{89}Sr) and samarium-153 (^{153}Sm) [4-7].

These radioactive isotopes localize to regions of enhanced bone turnover and deliver high local doses of radiation through the emission of β-particles.

The mechanism of bone targeting varies for each radioactive isotope. ^{32}P is targeted to bone through inorganic phosphate pathways. ^{89}Sr is taken up as a calcium analog. ^{153}Sm targeted to bone via chelation with phosphonic acid. The relevant nuclear decay properties of these radioactive isotopes are shown in Tab. 1.

Table 1. *Nuclear decay properties of radionuclides approved for treatment of metastatic bone pain*

radioisotopes	half-life, days	β-emission, average, MeV	penetration, mm	γ-emission, keV, %
Phosphorus-32	14.3	0.7	2.7	none
Strontium-89	50.5	0.58	2.4	none
Samarium-153	1.9	0.22	0.55	103, 29

The half-life and particle energy play a significant role in the clinical characteristics of these agents, such as onset and duration of palliative effects and time to recovery from myelosuppression. The particle emission from ^{32}P and ^{89}Sr and the corresponding ranges in bone and soft tissue are greater than for ^{153}Sm.

High-energy particles are associated with greater marrow toxicity, as a result of the large volumes of marrow exposed to radiation. The shorter physical half-life of ^{153}Sm (1.9 days) results in more rapid delivery of radiation than either ^{32}P (14.3 days) or ^{89}Sr (50.5 days).

For many patients with multiple symptomatic osteoblastic bone metastases who have relapsed following an initial course of hormonal or chemotherapy, bone-targeted systemic radioisotopes have emerged as a viable treatment option. The indications and contraindication for the use of bone-targeted radioisotopes are presented in Tab. 2.

Delivery of 90% of the total dose of radiation requires approximately 3.5 half-lives of decay, a time interval of approximately 1 week for ^{153}Sm, 7 weeks for ^{32}P, and 25 weeks for ^{89}Sr.

As a rule, ^{153}Sm is produced by the neutron bom-

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bardment of isotopically enriched $^{152}Sm_2O_3$ in a nuclear reactor.

Table 2. *Use of bone-targeted radionuclides for treatment of metastatic bone pain*

Indications	Relative contraindications	Absolute contraindications
Bone scan positive (osteoblastic lesions)	Predominant soft-tissue pain	Severe marrow suppression
Bone pain due to cancer	Unifocal bone lesions	Severe renal dysfunction
Multifocal disease	Osteolytic lesions (poor uptake on bone scan)	

2. CLINICAL-DOSIMETRIC CHARACTER ^{153}Sm

^{153}Sm oxabiphor was produced by "Radiopreparation"(Tashkent, Uzbekistan), the certificate of quality No.85, series No.026251114, with purity of >99.2%. Activity of ^{153}Sm oxabiphor was 2000 MBq. The initial activity of ^{153}Sm oxabiphor was 8400 MBq. The content of trace radioisotopes was not more $3{\cdot}10^{-3}$%. The content of Sm 62.0 μg/ml. The non-active trace element was absent. The content Na oxabiphor was 16.2 mg/ml, NaCl – 5.1 mg/ml. The radio preparation ^{153}Sm oxabiphor was sterile. Index hydrogen (pH) was 6.4.

This complex combination of Sm and oxa-bis(ethylenedithio)tetramethylphosphonium acid (Fig.1) has the biologic properties necessary for a bone-targeted radiotherapeutic agent.

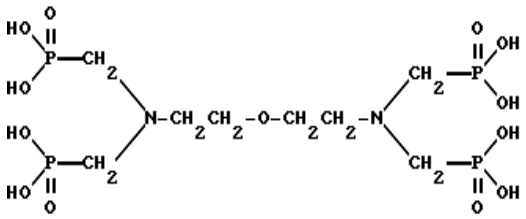

Fig.1. *The structure of the oxa-bis(ethylenedithio)tetramethylphosphonium acid*

3. CLINICAL STUDIES

These studies have been carried out on patients with painful bone metastases with a variety of primary tumors in the department of nuclear medicine of the Kharkov Institute of Medical Radiology. The majority of the patients had either primary prostate or breast cancer. Primary diagnostic bone scans are useful for identifying patients eligible for treatment with ^{153}Sm oxabiphor. Patients with symptomatic bone metastases were treated with single and repeat doses ranging from 0.28 mCi/kg to 0.84 mCi/kg. Standard dose of ^{153}Sm oxabiphor was 1 mCi/kg. This dose is safe and efficient. The injection of ^{153}Sm oxabiphor is simple and does not demands high technological equipment.

4. RESULTS AND DISCUSSION

Gamma spectrum for ^{153}Sm oxabiphor was measured by Ge(Li)-detector, volume 50 cm^3 with the energy resolution 3.25 keV on line ^{60}Co 1332 keV. Ge(Li)-detector was equipped by three-layer (Pb-Cu-Al) background protector (Fig.2).

Dynamics of ^{153}Sm content in a blood is characterized by average effective half-life $T_{1/2}$=0.68 hours [8]. The kinetics of ^{153}Sm oxabiphor in an organism with bone metastasis is specific for each patient. Radioactivity isn't being localized to the skeleton rapidly. This radio preparation is being cleared via the urine with complete excretion in 6 hours.

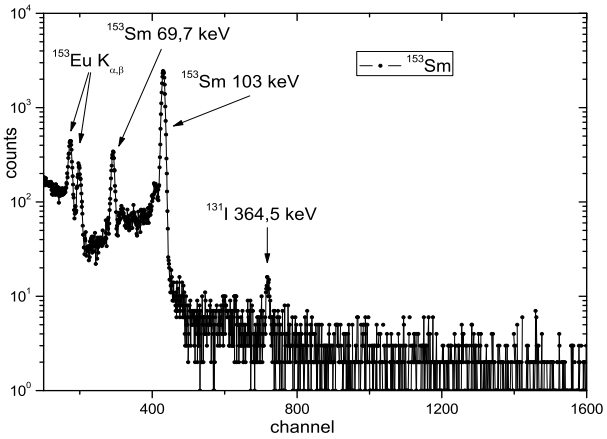

Fig.2. *The gamma spectrum of blood of patient during treatment by ^{153}Sm oxabiphor*

The preparation of ^{153}Sm oxabiphor was introduced intravenously. The medical dose was calculated by means of the use of specific value 1 mCi on kg of mass of the patient. Blood was taken (2 ml) at 3 days and 10 days during treatment of patients. The specific activity of a blood of patients in the course of treatment is given in Tab.3.

Table 3. *The activity A3, A10 of blood after treatment of ^{153}Sm oxabiphor after 3 and 10 days, respectively*

Bone metastases after cancer	A3 Bq/ml	A10 Bq/ml	Ratio A3:A10
L., Bile ducts	63.2	29.9	2.11
Si., Stomach	40.8		
Su., Prostate	13.2	9.7	1.36

It is possible to see that the concentration of ^{153}Sm oxabiphor in a blood of patients is decreased insignificantly. The effective half-life ^{153}Sm oxabiphor from a liver, kidney, and bladder 1.51, 11.9 hours and 3.1 days, accordingly [8]. Also the effective half-lives of a small amount of ^{153}Sm 22 and 29 days for a liver and nephroses, accordingly, are known. It is known that the effective half-life of ^{153}Sm from a bone tissue is 2.5 years. Apparently the lowering of

content of radiopharmpreparation at the patient of L. was caused by accumulation of a considerable amount of ^{153}Sm oxabiphor in a liver.

5. CONCLUSIONS

The concentration of ^{153}Sm oxabiphor in the blood of patients with bone metastasis during radionuclide therapy was determined. Variation of content of ^{153}Sm oxabiphor in the blood in patients with different primary disease was detected. The activity value of ^{153}Sm in blood of patients on the third day of treatment was in the range $6.9{\cdot}10^{-3}$% ... $3.3{\cdot}10^{-2}$% relative to the administered dose of the radiopharmaceutical. Later on the effective half-life of ^{153}Sm in the blood of patients depends on the localization of the tumor and is more than 7 days.

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КИНЕТИКА СОДЕРЖАНИЯ ^{153}Sm ОКСАБИФОРА В КРОВИ ОНКОБОЛЬНЫХ В КОМПЛЕКСНОЙ ТЕРАПИИ КОСТНЫХ МЕТАСТАЗОВ

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Определена концентрация ^{153}Sm в крови пациентов с метастазами в костной ткани после радионуклидной терапии. Обнаружена значительная вариация содержания ^{153}Sm в крови для больных с различными первичными заболеваниями, которая составила от 10 до 65 Бк/мл. Оценен период полувыведения ^{153}Sm из крови пациентов в процессе терапии, составляющий более 10 дней.

КІНЕТИКА ВМІСТУ ^{153}Sm ОКСАБІФОРУ В КРОВІ ОНКОХВОРИХ У КОМПЛЕКСНІЙ ТЕРАПІЇ КІСТКОВИХ МЕТАСТАЗІВ

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Визначено концентрацію ^{153}Sm у крові пацієнтів з метастазами в кістковій тканині після радіонуклідної терапії. Виявлено значну варіацію вмісту ^{153}Sm у крові для хворих з різними первинними захворюваннями, що склала від 10 до 65 Бк/мл. Оцінено період напіввиведення ^{153}Sm із крові пацієнтів у процесі терапії, що складає більш 10 днів.