HISTORY OF THE DEVELOPMENT OF THERAPY FOR MALIGNANT TUMORS

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Annotation: *In this article describes history of the development of therapy for malignant tumors. The development of highly effective means and methods for combating tumor disease is one of the cardinal tasks of public health. Among them, a special place is occupied by the creation and introduction into medical practice of highly effective drugs for the treatment of oncological diseases.*

Keywords: *malignant, tumor, modern medicine, cancer.*

The problem of malignant neoplasms, despite the significant advances achieved in the study of the tumor process, the development of methods of prevention, diagnosis and treatment, is still one of the most important in modern medicine. Among the causes of death, malignant tumors and neoplastic diseases of hematopoietic and lymphoid tissues, according to world statistics, rank second in highly developed countries. Although there are significant advances in the diagnosis and treatment of tumors, the number of cancer patients is quite large. This is due to an increase in the number of carcinogenic factors contained in the human environment, insufficient knowledge of the fundamental nature of the tumor process, the essence of the reasons for the transformation of a normal cell into a tumor, the pathogenesis of neoplasms, as well as the conditions conducive to their development.

Bis-(β-chloroethyl) amine derivatives were among the first to be used as antitumor agents.

The reason for the use of these compounds was the data obtained in the 40s of the XX century, during the Second World War, when the effect on the body of chemical warfare agents was studied in detail: mustard gas (or bis-β-

chloroethyl sulfide) and nitrogen mustard gas (or trichlorethylamine). Earlier, in 1919, it was established that trichlorethylamine causes severe leukopenia and bone marrow aplasia. Further studies have shown that trichlorethylamine has a specific cytotoxic effect on lymphoid tissues and has antitumor activity in lymphosarcoma in mice. Clinical trials of trichlorethylamine began in 1942, marking the beginning of the era of modern tumor chemotherapy.

The synthesis of bis- (β-chloroethyl) amine derivatives was first carried out at the end of the 19th century; however, it was only after the Second World War that the possibility of using these compounds in diseases of the hematopoietic system was shown and a new field of medical and chemical sciences - chemotherapy of malignant neoplasms - was practically initiated.

By 1950-1953, about 500 chloroethylamines were synthesized, but at that time some of them were used only as additional therapeutic agents in surgical intervention. Their limited use was explained by the fact that chloroethylamines, suppressing the growth of tumors, act simultaneously on all rapidly dividing cells. Since 1955, researchers have been synthesizing numerous derivatives of haloethylamines in order to obtain compounds with greater selectivity of action against tumors. If by 1960 more than 2000 derivatives of haloethylamines were obtained, by 1978 the number of these compounds synthesized in order to study their antitumor and antileukemic activity exceeded 3000.

Based on this system, all drugs are divided into groups according to their chemical composition, has a clear hierarchical structure, which facilitates its use for scientists, chemists and pharmaceutical industry, as well as further research in this area. Each medicine has its own chemical properties. In order to avoid undesirable consequences before the synthesis of new drugs and the improvement of existing ones, this classification is a convenient guide. Antineoplastic agents:

1. Synthetic: A) halogenated; B) containing an organic functional group; B) metal-containing; D) mixed.

2. Semi-synthetic and of plant and animal origin: A) antibiotics; B) alkaloids; C) enzymes; D) hormones.

3.Radioactive nucleides.

One of the first drugs based on chlorine was used as an antitumor agent from halogenated compounds. Subsequently, with further research, other halogens, such as bromine and fluorine, were used to reduce the toxic effect on the body.

Chlorethylamines are the most important halogen-containing drugs characterized by high reactivity.

Chlorethylamines of the aliphatic series. A characteristic feature of aliphatic chloroethylamines in aqueous solutions is rapid ionization with cyclization.

The mechanism of interaction of aliphatic chloroethylamines with nucleophilic agents depends on the polarity (dielectric constant) of the solvent and on the nucleophilicity of the attacking group.

Aliphatic bis- (β-chloroethyl) amines, for example, embihin, when dissolved in water, form an ethyleneimmonium cation at a lower rate than monochloroethyl amines.

A feature of these compounds is that the second electrophilic center in their molecule can react only after the opening of the first ethylene ammonium ion.

The first drug from the group of aliphatic chloroethylamines, which has been used for a long time in the oncological practice of our country, was embikhin. Due to its high toxicity, it was discontinued and replaced by a less toxic drug, novembichin. In many foreign countries, embihin is produced and used for the treatment of tumors at the present time.

In order to obtain less toxic drugs with greater selectivity of action on solid tumors, the researchers followed the path of replacing chlorine in the haloalkyl groups of aliphatic chloroethylamines with other halogens (bromine, iodine, fluorine).

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