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V. M. Perez-Garcia, S. Fitzpatrick, M. Pesic, P. Schucht, J. M. Sepulveda, F. M. Vallette. Applied mathematics in oncology. How can we help cancer patients? / V. M. Perez-Garsiya, S. Ficpatrik, M. Pesich, P. SHuht, ZH. M. Sepulveda, F.M. Vallett. Prikladna matematika v onkologiyi. YAk mi mozhemo dopomogti hovorim na rak?

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PREVENTION OF THE DEVELOPMENT OF THE SIDE EFFECTS DURING USING DEXAMETHASONE (EXPERIMENTAL STUDY)

Introduction. World Health Organization (WHO) Director-General Tedros Adan Ghebreyesus has named dexamethasone as the only effective drug for severe cases of COVID-19. Already in June 2020, Gebreyesus called for an increase in the production of dexamethasone for the treatment of severe patients. On 2 September 2020, WHO issued an interim guideline for the use of dexamethasone based on evidence from seven clinical trials. The document contains two recommendations: WHO strongly recommends oral or intramuscular administration of corticosteroids (dexamethasone) for the treatment of patients with severe and critical COVID-19; the regimen and duration of the course is carried out once a day for 7-10 days at a dose of 6 mg [1].

But dexamethasone is often used experimentally by physicians and biologists to simulate steroidal diabetes. Along with the stimulation of glyconeogenesis in the liver, dexamethasone inhibits glucose oxidation, enhances the breakdown of proteins, and inhibits their synthesis. With an increased release of amino acids from tissues and their entry into the liver, the process of transamination and deamination of amino acids, which are used for gluconeogenesis, is significantly accelerated. The

combination of these effects leads to the development of hyperglycemia and other manifestations of the so-called steroidal diabetes mellitus [2: 538].

There is a need to anticipate and prevent the negative effects of dexamethasone in the proposed dose on the structure of the main target organs. As a publicly available, inexpensive, and almost harmless remedy, we chose a decoction of blueberry leaves (*Vaccinium myrtillus*) [3: 316].

The aim of the paper is to study the organ protective effect of a decoction of blueberry leaves at the experimental use of dexamethasone at the recommended WHO therapeutic dose for the treatment of patients with COVID-19.

Materials and methods. Experimental studies were performed at thirty white male outbred laboratory rats (with an initial weight of 200 g) kept on the standard diet of the vivarium of Vinnitsia Pirogov Memorial National Medical University, which were divided into three groups: intact, animals injected intramuscularly with dexamethasone 36 mg (which corresponds to a dose of 6 mg for humans) for 10 days [1] and rats, which on the background of the introduction of dexamethasone injected a decoction of blueberry leaves - *Vaccinium myrtillus* (1:5 1 ml per 100 g of mass intragastrically) also for 10 days. Rats were kept under standard vivarium conditions at 12-hour day lighting, air temperature - 20-25°C, air humidity - 50-55%. All manipulations with animals were carried out according to the positions of "European Convention for the Protection of Vertebrate Animals used for experimental and scientific purposes" (Strasbourg, 1986) [4] and the regulation IV National Congress on Bioethics (Kyiv, 2010) [5]. Histological examinations were performed according to the generally accepted method.

Results of the research. The animals were slaughtered under light ether anesthesia. For morphological studies, the right lateral lobe of the liver was constantly taken. Experimental administration of dexamethasone resulted in a preserved lobular structure observed in the liver tissue, but in the centrilobular zone there were areas where the radial location of the liver plates was disturbed, sinusoidal capillaries were significantly dilated.

Hepatocytes in such areas were often nuclear-free, optically vacuolated. In hepatocytes with preserved nuclei, their edema and hyperchromia were noted. Some cells had a swollen cytoplasm with a large number of optically empty vacuoles. In the centrilobular zone, there were also isolated foci of hepatocyte necrosis with infiltration of a large number of lymphocytes. Thrombi were observed in dilated lumens of sinusoidal capillaries and central veins. Endothelial cells of sinusoidal capillaries were inhomogeneously stained. Dystrophy and necrosis of hepatocytes were noted in the periportal zone. Dystrophy was fatty degeneration of hepatocytes (Fig.1(a), 1(b)).

Prophylactic administration of blueberry decoction contributed to the fact that the negative changes were significantly offset. Microscopic light-optical examination of the liver tissue of rats of the group with the prevention of aggressive effects of dexamethasone showed a slight violation of the structure of the liver plates, a slight expansion of the space of sinusoidal capillaries, a decrease in the number of

macrophages, lymphocytes. Hepatocytes had a homogeneous cytoplasm, only some had optically empty vacuoles (Fig.1(c))

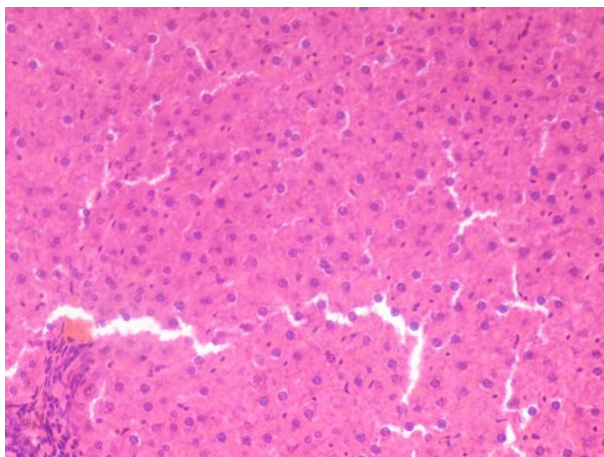


Fig.1(a) Histological examination of the liver tissue of the rat of the intact group. x200

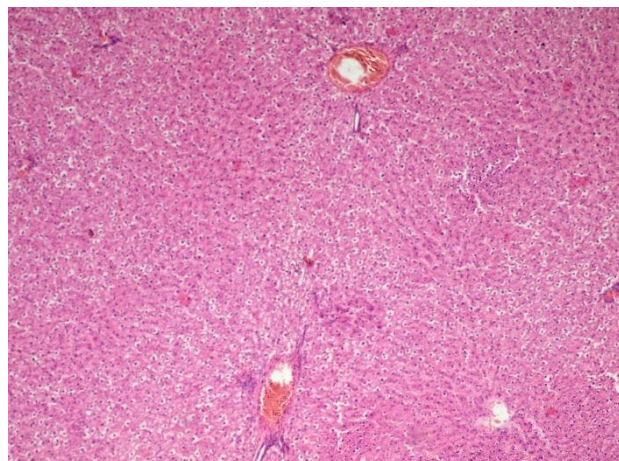


Fig. 1(b) Histological examination of the liver tissue of dexamethasone group. x200

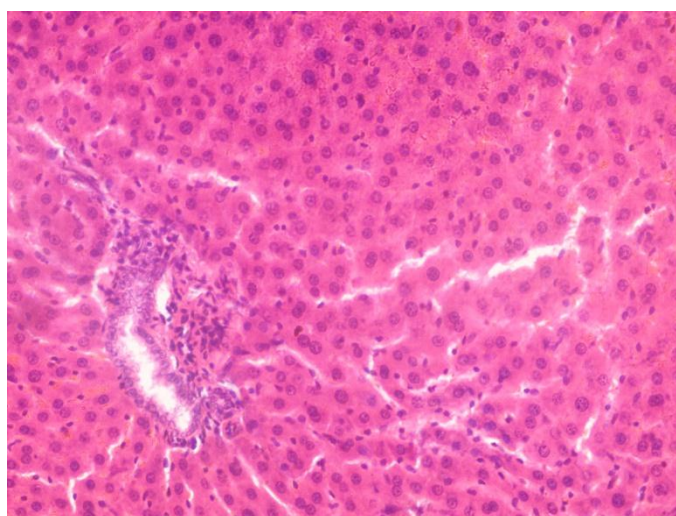


Fig.1(c). Histological examination of the liver tissue of dexamethasone group, prevention. x100

Conclusions. Intramuscular administration of dexamethasone at a dose of 36 mg/daily for 10 days (according to WHO recommendations for patients with COVID -19) causes severe dystrophic changes in the liver. At the same time taking a prophylactic agent – a decoction of blueberry leaves in a dose of 1:5 per 100g has a pronounced organ protective effect.

We consider it expedient to further study the effect of dexamethasone in the proposed dose on the morphology and physiology of the most important organs and organ systems and means of prevention of side effects of this drug.

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BRAIN STIMULATION THERAPIES

Introduction. Mental disorders are one of the most difficult medical problems affecting people around the world. These changes can directly or indirectly affect a person's lifestyle in society, his ability to work, the ability to perform daily tasks, and adequately perceive events around him. Brain stimulation therapy plays an important role in the diagnosis and treatment of mental defects.

Brain stimulation therapy aims at activation or inhibition of the brain activity directly by electricity. The electricity itself can be supplied by electrodes that are implanted in the brain or non-invasively through electrodes placed on the scalp [1]. Although these therapies are used less frequently than drug treatment; they treat mental disorders that are not treated with medication and other treatments.