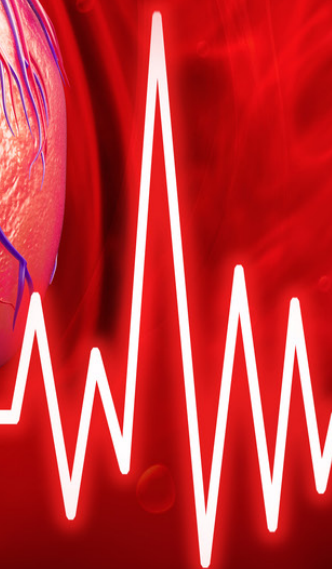
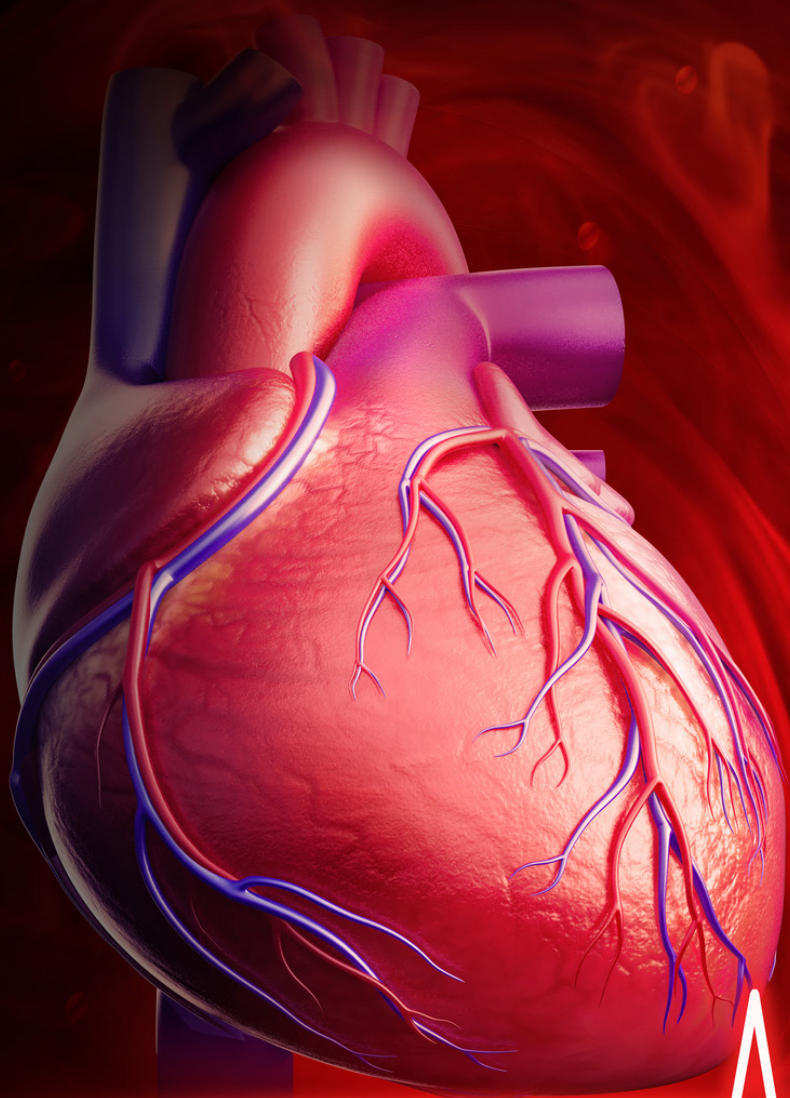


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INFLUENCE OF KOBAVIT ON THE ACTIVITY OF THE MONOOXYGENASE SYSTEM IN WOMEN WITH UTERINE FIBROIDS

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Key words: Uterine fibroids, Synthetic progestins, MOS, Pharmacokinetics of Antipyrine, Kobavit, Hepatoprotector

Abstract: Taking into account the insufficient effectiveness of conservative therapy for uterine fibroids, non-surgical treatment of uterine fibroids was attempted with the use of Kobavit. At the same time, special attention was paid to the detoxifying potency of the liver - MOS. The study was conducted in 33 patients with a verified diagnosis of uterine fibroids, who were divided into 2 groups, one of which received Narcolut, the other Narcolut with Kobavit. The detoxifying potency of the liver was judged by the pharmacokinetic parameters of antipyrine. The results of the study showed that there is a significant inhibition of the function of MOS activity in patients with uterine fibroids. Narkolut does not lead to the complete elimination of violations of the MOS. In order to increase the effectiveness of conservative treatment of uterine fibroids, it is advisable to combine the use of synthetic progestins with cobavit.

Introduction.

The development of effective methods for the treatment of benign hyperplastic diseases of the organs of the reproductive system is extremely relevant, because despite the increase in the arsenal of hormonal drugs used in gynecological practice, as well as the expansion of possibilities for the use of non-drug methods, treatment results are not always quite effective (1,2,3). This is probably due to the complex mechanisms of the pathogenesis of the development of pathological conditions of the organs of the reproductive system against the background of multisystem damage to the body of women.

In the conservative treatment of patients with uterine fibroids, a significant role is played by synthetic progestins, since the point of view about estrogen stimulation of tumor growth is well known (5,6) However, their use is accompanied by a noticeable inhibition of the absorption-excretory, protein and fat-lipid functions of the liver (6,7). Based on this, on the days of taking non-steroidal series of drugs, in order to prevent

possible side effects of medications, it is recommended to prescribe protectors of the gastrointestinal-hepatic complex (6,7). The above served as the basis for conducting this study, the purpose of which was to study the effect of the combined use of kobavit on the monooxygenase system (MOS) of the liver - the main system providing the metabolic functions of the organ in women with uterine fibroids. Kobavit, as is known, is a domestic hepatoprotector (9), chemically it is a complex compound of trivalent cobalt with vitamin U and glutamic acid (9). It has the properties of improving lymphopoiesis, immunity in anemia of 1st and 2nd degrees (10).

The main part.

Under observation were 33 sick women aged from 35 to 57 years (with an average age of 43.8 ± 0.6 years. The duration of the disease from first diagnosis ranged from a few months to six years) with a verified diagnosis of uterine fibroids. In five patients, myoma size did not exceed 6-8 weeks of pregnancy, while in three patients, it was found at 10-11 weeks (9.1%). Most of the patients examined had a body weight slightly above the physiological norm (first-degree obesity).

The menstrual cycle had an average of 28-30 days, and menstruation lasted for five or more days, often accompanied by heavy bleeding. Reproductive activity was preserved in all cases, but infertility was found in the anamnesis of three women: primary infertility in two (three years and five years) and secondary infertility in one woman (more than six years). Out of all those examined, only two women had 2-3 pregnancies, while 13 women had 4-5 pregnancies. Multiple births (three or more births) were reported by 18 women (54.55%). Of these women, 81% had 1st grade of anemia, 46.2% had respiratory system pathologies, 54% had gastrointestinal system diseases, and 30.8% suffered from diseases of the hepatobiliary system.

The functional activity of MOS was assessed based on the antipyrine test, which was performed twice: at the first visit of patients after diagnosis and after conservative treatment.

The patients were divided into two groups according to the principle of random selection. Both groups were comparable in age, diagnosis, concomitant extragenital diseases, and race. In patients of the first group, treatment was carried by Narkolut 0.5g one time a day during 20 days. Second group along with this additionally received kobavit 0.01g 2 times a day during 20 days. The study of pharmacokinetic parameters (PK) of antipyrine was always carried out in the morning, after administration of antipyrine orally at a dose of 10 mg/kg (1% solution of the drug at the rate of 1 ml per 1 kg of body weight). In the blood serum taken after 3, 12 and 24 hours, the content of antipyrine was determined by using the spectrophotometric method. The values of $T_{1/2}$, aV_d , MCP, AUS were calculated using previous methods (13). The results obtained were compared with the data of a group consisting of 6 practically healthy women of

the appropriate age who were familiarized with the purpose of follow-up. The figures data were processed by the method of variation statistics.

Table 1

The influence of complex treatment with the inclusion of cobavit on the pharmacokinetic parameters of antipyrine in patients with uterine fibroids

Groups	$T_{1/2}$, h	aVd ml/kg	MCR ml/kg.h	k_{el} h ⁻¹	AUS, mkg/min. ml
Healthy	9,0 ± 0,86	536,9 ± 75,8	40,8 ± 2,59	0,08066 ± 0,00772	250,8 ± 17,7
Uterine fibroids: on admission	18,7 ± 1,0*	592,9 ± 25,3	23,2 ± 1,19*	0,04038 ± 0,00222*	473,1 ± 35,6*
after treatment	<u>16,0 ± 0,93*</u> 12,0 ± 0,92**	<u>490,7 ± 38,8#</u> 584,1 ± 57,7	<u>22,0 ± 2,01*</u> 36,8 ± 4,79#	<u>0,04540 ± 0,00346*</u> 0,05833 ± 0,00457**	<u>491,9 ± 43,9*</u> 319,0 ± 33,0#

Note: * - statistically significant differences compared to healthy individuals.

--compared to data upon admission to the clinic.

in the numerator – the results obtained in patients treated with synthetic progestins.

in the denominator – data from patients additionally receiving cobavit.

The data obtained showed that uterine fibroids are accompanied by viral significant violations of antipyrine *PK* parameters. Thus, compared with healthy individuals, the value of the half-life of distribution ($T_{1/2}$) is extended by 107.8%, the area under the pharmacokinetic curve (S) - by 89%. At the same time, the value of metabolic clearance (*MCR*) and elimination constant (*K_{el}*) were measured to be 43.2 and 50%, respectively. Against this background, the value of the current volume of distribution (*aVd*) does not undergo statistically significant changes (see table 1). The revealed violations of the *PK* of antipyrine clearly indicate inhibition of the functional state of the MOS in patients with uterine fibroids. Since antipyrine is quickly and completely absorbed from the digestive system, it is distributed evenly throughout the entire liquid environment of the body, slightly binds to tissue and plasma proteins and is completely metabolized with the participation of cytochrome P-450 123 isoforms (14,15). Therefore, the test with antipyrine has found wide use in clinical practice as the most reliable, simple and informative test in assessing the functional activity of the MOS. With low MOS activity, the oxidation of endogenous compounds, including hormones, slows down, and their concentrations in body fluids, and especially in the blood, increase, which causes an increase in their biological effect on target organs. Considering this circumstance,

it can be assumed that hyperestrogenemia observed in women with uterine masses may be the result of a decrease in biotransformation and a slowdown in the elimination of estrogens, under conditions of which their stimulating effect on the process of endo- and myometrial hyperplasia increases. Probably, from these considerations it is clear that the development of the uterine fibroids is often accompanied by a variety of metabolic disorders (6). Therefore, in managing patients with benign hyperplastic diseases of the uterus, special attention should be paid to the correction of concomitant metabolic problems due to extraginal pathology. This is an effective measure to prevent the development of neoplastic processes in the target organs of the reproductive system (3,4). As shown by the analysis of the variation series of the obtained results, the *PK* parameters of antipyrine in a number of patients were significantly violated, and were almost twice as high as the average value of group. These are patients who, in addition to uterine fibroids, were diagnosed with liver and lung pathologies on the background of varying degrees of anemia. It is believed that after hormonal therapy the state of the hepatobiliary system improves, however, a number of its functions remain impaired. Therefore, along with hormonal therapy, women with benign hyperplastic processes of the uterus must be prescribed hepatoprotective agents. uterus, it is not necessary to prescribe hepatoprotective agents (7). Moreover, for the purpose of warning norsteroid series possible side effects of using drugs and it is recommended to prescribe gastric protectors gastro-intestinal complex (6). Considering the above, it was of great interest in using cobavit against the background of hormonal therapy for uterine fibroids, the effectiveness of treatment, as well as on the functional state of the MOS system.

The results of the study showed that after hormone therapy antipyrine PK indicators only tended to recover, since there were clear impairments compared to the level of healthy individuals. Thus, the values of $T_{1/2}$ and S were increased by 77.5 and 96.1%, and the decrease in the MCR value was by 46.1 and 43.7%. It can be seen that there were no statistically significant changes after hormone therapy in patients compared to the initial values. Moreover, some parameters (MCR, S) even worsened. Consequently, hormonal therapy does not have a restorative effect on the functional activity of the MOS. This conclusion is in accordance with the data of other researchers who have established the negative effect of hormone therapy on the metabolic functions of the liver in uterine fibroids (4,7). A different picture of changes in antipyrine PK disturbances was observed in patients receiving additionally Kobavit. Thus, the values of $T_{1/2}$ and S decreased by 25 and 35.1%, and the values of MCR and K_{el} , on the contrary, increased by 67.3 and 28.5%, respectively, compared to the control group of patients not taking this hepatoprotector. As can be seen from the data given in table 1 in treated women with Kobavit clearly restored a number of parameters of the pharmacokinetics of antipyrine. Consequently, the use of cobavit together with synthetic progestins in patients with uterine fibroids allows the restoration of the functional activity of the liver MOS, which plays an important role in the processes of biological transformation and con-

jugation of xenobiotics and endogenous physiologically active substances, including sex hormones. This conclusion is in good agreement with the data of researchers who have established the stimulating effect of cobavit on a number of metabolic processes occurring in the liver, such as bile formation (8), metabolism of carbohydrates (11) and lipids (10). Moreover, in case of liver pathologies, this cobalt coordination compound was not inferior in its effectiveness to the well-known hepatoprotectors Essentiale and Silbor. Probably, when using cobavit, the elimination of violations of these types of metabolism is the result of the restoration of the functional activity of the MOS because it plays a central role in these processes. Analysis of the results of a study of the pharmacokinetics of antipyrine revealed that the positive effect of cobavit on the functional activity of MOS was more pronounced in women taking this drug against the background of megistron than in narcolut. At the same time, in the group of patients treated only with synthetic progestins, the degree of disturbances in the pharmacokinetics of antipyrine remained to a higher degree, especially in women receiving narcolut. The latter, although in the majority of patients normalized the clinical manifestations of fibroids (menstrual cycle, volume of blood loss, painful sensations during menstruation, etc.), however, had a negative effect on the liver. This is probably due to the fact that the drug has an inhibitory effect on synthetic processes not only in the ovaries, but also in other organs, including the liver. Therefore, when using narcolut, careful monitoring of the condition of the liver is recommended (7,6). Consequently, the functional activity of MOS, judging by the antipyrine test, is significantly inhibited in uterine fibroids, and treatment with synthetic progestins does not eliminate it. At the same time, the combined use of cobavit with narcolut, and especially migistron, leads to a clear restoration of the detoxifying potency of the liver and has a beneficial effect on the course of the disease. It should be noted that the restoration of the intensity of the processes of biotransformation of endo- and exogenous chemical substances in hepatocytes under the conditions of the use of cobavit probably enhances the metabolism and conjugation of sex hormones, which play a major role in the pathogenesis of the development of uterine fibroids.

Conclusion.

1. With uterine fibroids, the functional state of the MOS is clearly depressed.
2. Treatment with synthetic progestins does not eliminate MOC disorders.
3. The hepatoprotector cobavit is the drug of choice in the correction of disturbances in the detoxifying function of the liver in uterine fibroids.
4. In order to increase the effectiveness of conservative treatment of uterine fibroids, it is advisable to combine the use of synthetic progestins with cobavit

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THE EFFECT OF HYDROCORTISONE ON BONE MARROW IN ONTOGENESIS

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Аннотация

В статье представлена информация о применении кортикостероидных гормонов в клинике без учета генетической индивидуальности, сформированной в длительном процессе филогенеза, часто приводит к серьезным осложнениям. Устранить их будет возможно после глубокого сравнительного анализа гормонозависимых процессов иммуногенеза целостного организма. Раскрытие закономерностей ответной реакции иммунной системы черепах различного возраста на действие кортикостероидных гормонов, показанные на системном, клеточном и ультраструктурном уровнях позволяют дополнить механизмы патогенеза стресса, известные у млекопитающих и человека.

Ключевые слова: Иммуногенез, онтогенез, костный мозг, стресс, гидрокортизон, возраст, патогенез, млекопитающие, организм, ответная реакция, процесс.

INTRODUCTION

Compensatory and adaptive processes in the human and animal body to extreme environmental influences are closely associated with the immune status of the organism. The functional activity of the organs of the immune system is simultaneously under the regulatory influence of the neuroendocrine system, particularly the hormones of the adrenal glands. It has been established that adrenal cortex hormones participate in the mechanisms of seasonal biorhythms of immune system activity; moreover, it has been shown that small doses stimulate it, while large doses suppress it.

As is well known, a proper understanding of the formation processes of various structures of hematopoietic tissue can be achieved only through comparative and evolutionary studies of their ontogenesis—starting from the simplest chordate animals and progressing through fish, amphibians, reptiles, birds, mammals, and finally, to humans.

Reptiles are the first representatives of the amniotic group of vertebrates that possess a stable pulmonary type of respiration and lead a terrestrial lifestyle, while still being poikilothermic animals. They occupy a key position in the evolutionary lineage of vertebrates, as they are the ancestors of birds and mammals. The formation of the immune system in reptiles does not end during embryogenesis; after hatching, this process continues under the direct control of various types of hormones and tissue regulators.

MATERIALS AND METHODS OF RESEARCH

The object of our study was representatives of the reptile class — the Central Asian tortoise *Testudo horsfieldii*, which belongs to the order Chelonia. In the experiment, we used young individuals (hatchlings) weighing 30–90 g, sexually mature individuals weighing 200–250 g, and adults weighing 500–900 g, of both sexes. The animals were kept under laboratory conditions, with

the ambient temperature corresponding to the season. The Central Asian tortoise leads a sedentary lifestyle, entering a state of torpor during the winter period and awakening in March–April. It reaches sexual maturity at around ten years of age. The age of the tortoises was determined by the annual growth rings on the dorsal and ventral scutes of the shell.

Hydrocortisone (manufactured by Richter, Hungary) was administered intramuscularly into the thigh at a dose of 100 mg/kg of body weight, once during the spring-summer and autumn periods. The hormone dose was chosen based on literature data concerning the degree of lymphocyte elimination in the adrenal cortex of mammals and its effective impact on the organs of hemopoiesis and lymphopoiesis in lower vertebrates.

Control animals, kept under identical conditions, were injected with a 0.6% sodium chloride solution in a volume equal to that of the hormone suspension used in the experiment. The animals were euthanized by decapitation on the 9th–10th day after the administration of hydrocortisone, as the hormone reaches its maximum effect during this period.

For cytomorphological studies, samples of bone marrow were taken. For general morphological examinations, the material was fixed in Carnoy's fluid and 10% formalin, embedded in paraffin, and serial sections 3–5 μm thick were prepared. The paraffin sections were stained with hematoxylin and eosin (according to Karacci's method).

In addition, the fine structure of lymphoid organs and bone marrow was studied on semi-thin sections (1–2 μm). The organ samples were fixed in a 2.5% glutaraldehyde solution prepared in 0.1 M phosphate buffer with 1% sucrose added, for 90–120 minutes. After fixation in osmium tetroxide in the same buffer for 30–50 minutes, the samples were dehydrated in ascending concentrations of alcohol, then in absolute acetone, and embedded in a mixture of epon-araldite according to the standard technique (17). Sections (1–2 μm) prepared using an LKB-8800 ultratome were stained with 1% azure-eosin containing 1% borax for 5 minutes over an alcohol lamp flame.

RESEARCH

The bone marrow of reptiles is the main organ of hematopoiesis, where erythropoiesis, myelopoiesis, and lymphopoiesis occur throughout the entire postembryonic period. The lymphocytes formed in the bone marrow of reptiles represent a special population of B-lymphocytes responsible for the synthesis of immunoglobulins both under normal conditions and during antigenic stimulation. The unique microcirculatory system of the bone marrow is one of the most important components of its stroma: the walls of the bone marrow vessels form a barrier between the hematopoietic tissue and the bloodstream, providing conditions for the orderly migration of cellular elements. The stroma of the bone marrow, like that of other hematopoietic organs in reptiles, is composed of reticular cells and reticulin fibers, within whose loops the hematopoietic cells are located. Fat cells are often found in the bone marrow, and they constitute the main mass of the bone marrow cavity.

In amphibians and reptiles, during the winter period, hematopoietic bone marrow is normally replaced by fatty tissue, and in spring it is restored. Bone marrow stem cells are distributed throughout the organism, determining the development of various lymphoid elements. Therefore, the state of

the organism's immune system is defined by the combined activity of all structures involved in hemopoiesis and lymphopoiesis.

To date, it is firmly established that the main immunocompetent cellular elements responsible for the immune responses of the organism are T- and B-lymphocytes, their populations, as well as the macrophage cell system and granulocytes — all of which develop from hematopoietic stem cells. Although the existence of stem cells has been known for a long time, morphologically they are still not well characterized. Some authors suggest that small and medium lymphocytes, bone marrow monocytes, blast cells, and lymphocyte-like bone marrow cells may perform stem cell functions. Others believe that stem elements are cells distinct from both lymphocytes and the monocytic-macrophage cell line. It is thought that the pool of hematopoietic stem cells exists among the hydrocortisone-resistant lymphocyte-like cells of the bone marrow.

Interesting data have been obtained in studies of stem cell functions *in vitro*. When hematopoietic stem cells are cultured, colonies consisting of cells of a single histological type are formed: erythroid, granulocytic-macrophage, megakaryocytic colonies of T-lymphocytes, and colonies of B-lymphocytes.

The T-lymphocyte system is one of the most important components of immunity, responsible for mediating various reactions of cellular immunity. According to the generally accepted classification, the main populations of T-lymphocytes include T-helpers, T-killers, and T-suppressors. In addition to these subpopulations, other types of T-line cells have also been identified: T-amplifiers, T-initiators, X-differentiating lymphocytes, and T-regulators of helpers and suppressors. It has been established that the functional activity of T-suppressors is controlled by a special subpopulation known as “counter-suppressors.”

The population of B-cells, like that of T-cells, is heterogeneous. In addition to B-lymphocytes that transform into plasma cells secreting antibodies, B-cells with suppressive activity have also been identified.

Macrophages are the third type of cells involved in the implementation of the immune response. In addition to capturing antigens and presenting them in an immunogenic form to other immunocompetent cells, macrophages also perform a range of other functions. The thymus, likewise, is not a homogeneous organ in terms of T-cell composition. Memory B-cells have been identified in the thymus of mice. The thymus of animals contains about 0.5% to 3% of immunoglobulin-bearing cells. The above description of the main cellular elements of the immune system has been obtained from studies primarily conducted on mammals, mostly on inbred strains of mice.

The immune system of reptiles, in terms of its morphological and functional characteristics, occupies an intermediate position in phylogeny—between amphibians and birds on one side, and mammals on the other. Many aspects of reptilian immune system functioning remain insufficiently studied. There is still no clear understanding of all the cellular elements that carry out immunological reactions in the organism. The processes of immune regulation and the interconnections between the immune system and other physiological systems remain largely unknown.

In mammals, such lymphocytes are regarded as natural killer cells. A portion of small and medium lymphocytes undergo destructive changes, including nuclear pyknosis and cytoplasmic vacuolization. With a significant reduction in the number of lymphoid elements, mature plasma cells become evident, and macrophages show active erythrocyte destruction.

Bone marrow. As is known, in the peripheral blood of adult tortoises, at all observation periods following the administration of hydrocortisone at a dose of 100 mg/kg, there is a pronounced heterophilic leukocytosis and lymphopenia. It was noted that by the 10th day, the absolute number of karyocytes in the bone marrow begins to decrease—mainly due to the reduction of lymphoid elements. Our experiments showed that in hatchling tortoises, by the 10th day after hydrocortisone administration at the same dose, the number of cellular elements was sharply reduced (Fig. 1). This phenomenon is especially noticeable in the disappearance of lymphoid elements and their replacement by clusters of granulocytes within the bone marrow tissue (Fig. 2)

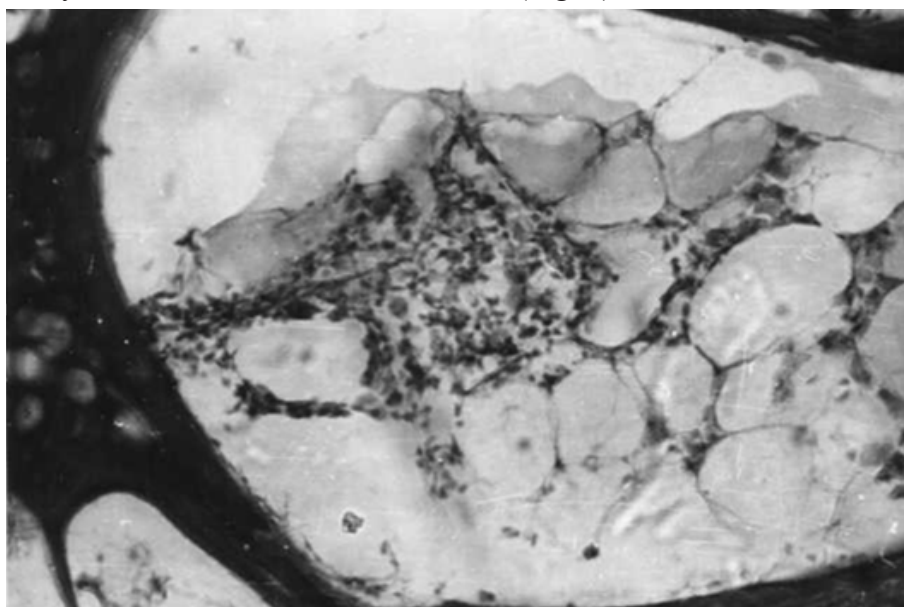


Fig. 1. Tortoise. Sexually mature. Bone marrow.
Reduction of hematopoietic islands. Magnification $\times 250$.

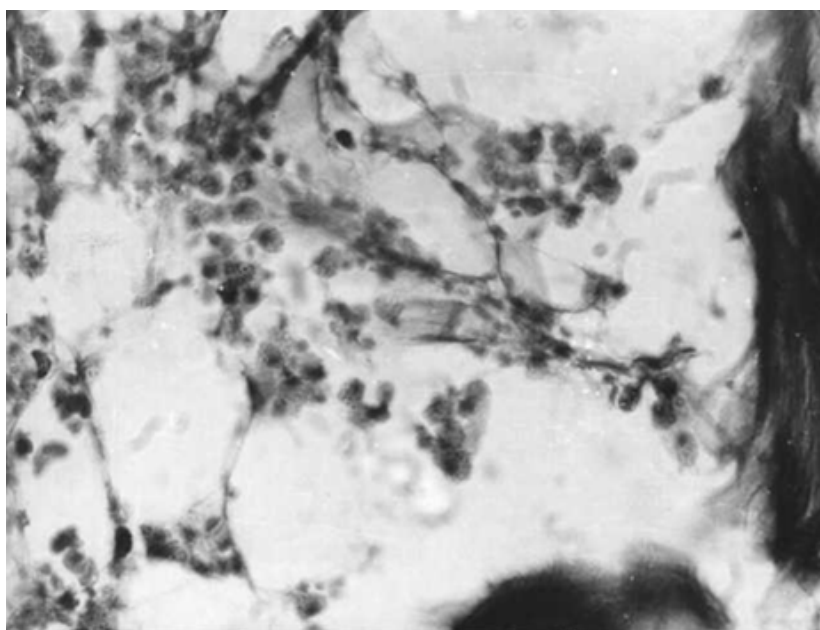


Fig. 2. Tortoise. Hatchling. Bone marrow.
Predominance of granulocytic series elements. Magnification $\times 500$.

An increase in the elements of the proliferative pool of granulocytes in tortoises of all ages

occurs due to a rise in the number of myeloblasts and promyelocytes. At the same time, there is an increase in the number of mature heterophilic elements. When analyzing bone marrow smears, a specific phenomenon characteristic of tortoise heterophils should be noted. In close proximity to the sinusoids, clasmocytosis of these cells occurs—most prominently in animals that received hydrocortisone (Fig. 3).

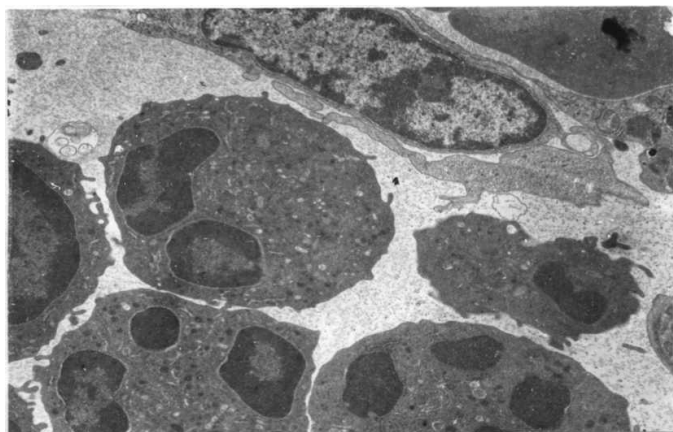


Fig. 3. Tortoise. Adult. Bone marrow.

Granulocytes after hydrocortisone administration. Magnification $\times 5,000$

In the cytoplasm of heterophils, cytoplasmic degranulation and an increase in the number of vacuoles are observed (Fig. 4).

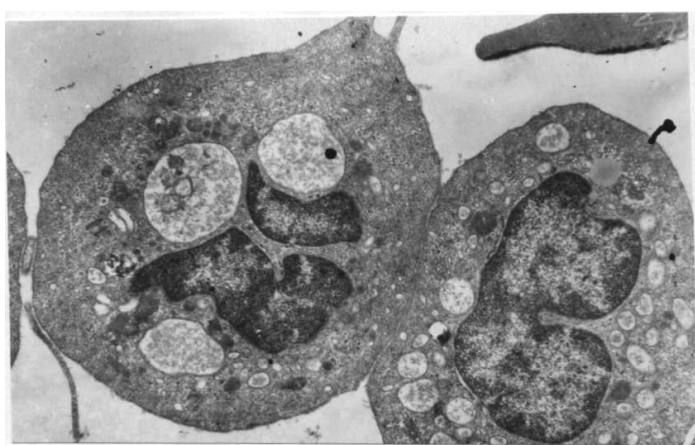


Fig. 4. Tortoise. Hatchling. Bone marrow.

After hydrocortisone administration. Heterophil. Magnification $\times 25,000$.

The biological essence of the processes occurring in the bone marrow of experimental animals lies in the organism's defensive response under conditions of lymphoid tissue damage: redistribution of lymphoid elements, including precursors of T- and B-cells, and activation of macro- and microphage reactions.

CONCLUSIONS

1. A single administration of hydrocortisone at a dose of 100 mg/kg causes significant

structural and functional changes in the bone marrow of Central Asian tortoises, including lymphocytopenia, suppression of proliferative processes in the thymus and bone marrow, and involution of the organism's lymphoid tissue.

2. The hormone-induced reaction of the bone marrow in young tortoises (hatchlings) is less pronounced: inhibition of lymphocytopoiesis in the thymus is observed only in the cortical substance, whereas in adults, destruction occurs in both the cortical and medullary regions. The lymphoid tissue of the bone marrow is less affected in younger animals.
3. Following a single exposure to hydrocortisone, by the 10th day, ultrastructural changes develop in the bone marrow cells, indicating a disruption of the organism's immunological functions.

Summary

The use of pharmacological doses of hydrocortisone (as a model of stress reaction) in tortoises at various stages of postnatal ontogenesis made it possible to identify both the mechanisms of hormone-dependent immune system responses common to all vertebrates and the specific species-related characteristics.

Moreover, the bone marrow response in young tortoises demonstrates a certain tolerance to hydrocortisone, which is likely associated with the delayed development of the receptor system and the biochemical peculiarities of immunocompetent cells.

The elucidation of the patterns of immune system responses in tortoises of different ages to the effects of corticosteroid hormones—observed at systemic, cellular, and ultrastructural levels—helps to expand the understanding of stress pathogenesis mechanisms known in mammals and humans.

The use of evolutionarily ancient animals, which occupy a lower level of biological development, provides an opportunity to reveal the fundamental processes underlying the formation of morpho-functional systems and immunogenesis during the progressive evolution of organisms in phylogeny. These findings may be applied in developing therapeutic protocols for the clinical use of corticosteroid hormones in practical medicine.

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QANDLI DIABET SHAROITIDA TALOQ BEZINING GISTOSTRUKTURAL VA MORFOFUNKSIONAL O'ZGARISHLARI

Toshkent davlat tibbiyot universiteti talabasi

Izzatullayeva Mehruza

Annotatsiya. Ushbu maqolada qandli diabet sharoitida taloqbezining gistostruktural va morfofunktsional o'zgarishlari o'rganildi. Diabet sharoitida organizmning immuno-biologik himoya tizimi faoliyatida sezilarli buzilishlar yuzaga kelishi, xususan, limfoid to'qimalarning atrofiya holatiga o'tishi, germinativ markazlarning qisqarishi, oq qon tanachalarining tarkibiy o'zgarishi va taloq kapillyarlarining morfometrik parametrlari kamayishi kuzatildi. Maqolada, shuningdek, taloqning qizil va oq pulpa zonalarida kechadigan gistostruktural buzilishlar, ularning to'qima regeneratsiyasi va funksional kompensator mexanizmlariga ta'siri ham yoritib beriladi. Olingan natijalar asosida qandli diabet fonida taloqdagi immunologik zaiflik va to'qimalarning degenerativ-distrofik o'zgarishlari bilan bog'liq morfologik o'zgarishlar xulosalandi. Ushbu ilmiy ish diabetik holatlarda organizmning immun tizimi faoliyatini chuqur tushunishga hissa qo'shadi hamda klinik va eksperimental morfologiya sohasida dolzarb muammolarni hal etishga yo'naltirilgan. Kalit so'zlar.

Qandli diabet, taloq bezi, metabolitik buzilish, plazma, gistostruktura, glyukoza almashinuvi, insulin, oqsil sintezi, qon zaxirasi, immun tanqislik, sinnusoid kapilyar, makrofag, autoimmun reaksiya, immunoglobulin, germinativ markaz, atrofiya, deginiratsiya

Kirish. Bugungi kunda qandli diabet (diabetes mellitus) global sog'liqni saqlash tizimi oldida turgan eng muhim va keng tarqalgan metabolik kasalliklardan biri hisoblanadi. Jahon sog'liqni saqlash tashkiloti (JSST) ma'lumotlariga ko'ra, dunyo bo'yicha qandli diabet bilan kasallanganlar soni yildan-yilga ortib bormoqda, xususan, 2045-yilgacha bu raqam 700 milliondan oshishi kutilmoqda. Ushbu surunkali kasallik faqatgina glyukoza almashinuvi bilan bog'liq muammolarni keltiribgina qolmay, balki organizmning barcha a'zolari va tizimlariga, ayniqsa qon-tomir, buyrak, asab va immun tizimlariga ham chuqur ta'sir ko'rsatadi. Qandli diabet sharoitida ro'y beradigan giperglikemiya, lipidlar va oqsillar almashinuvi buzilishi, oksidlovchi stress va yallig'lanish holatlari immun tizim faoliyatining susayishiga olib keladi. Organizmning immunologik himoyasi zaiflashgan holatlarda esa infeksiyon kasalliklar xavfi ortadi, yallig'lanishlarga qarshi kurashish mexanizmlari izdan chiqadi. Bu esa organizm uchun ikkilamchi asoratlar xavfini oshiradi. Shu nuqtai nazardan qaralganda, immun tizimining muhim tarkibiy qismi bo'lgan taloq bezining qandli diabet fonida qanday o'zgarishlarga uchrashi dolzarb ilmiy va amaliy masala sifatida qaralmoqda. Taloq (splen)

bezi – limfoid to‘qimalardan tashkil topgan, immun javob shakllanishida ishtirok etuvchi, eskirgan eritrotsitlar va qon elementlarini yo‘q qiluvchi, yangi limfotsitlar va antitanalar ishlab chiqarishda ishtirok etuvchi muhim a‘zolaridan biridir. Uning oq va qizil pulpa zonalarida turlicha morfologik va funksional faoliyatga ega bo‘lib, limfoid elementlarning proliferatsiyasi, fagotsitoz va immun monitoring funksiyalarini bajaradi. Taloqning ushbu murakkab faoliyati qandli diabet sharoitida sezilarli darajada buzilishi mumkin. So‘nggi yillarda olib borilgan ilmiy izlanishlar qandli diabet sharoitida taloqning gistostruktural o‘zgarishini ko‘rsatmoqda. Xususan, oq pulpa zonasining qisqarishi, limfoid to‘qimalarning regressiyasi, germinativ markazlarning yo‘qolishi, kapillyarlarning devorlarida degenerativ-distrofik holatlar, makrofag va limfotsitlar tarkibining buzilishi kabi o‘zgarishlar qayd etilgan.

Ammo bu boradagi ilmiy ma‘lumotlar ko‘proq tajriba hayvonlari asosida o‘rganilgan bo‘lib, ularni umumlashtirish, klinik va eksperimental jihatdan chuqur tahlil qilish hamda morfologik asoslarini yoritish dolzarb muammoligicha qolmoqda. Ushbu tadqiqot aynan shunday bo‘shliqlarni to‘ldirishga, qandli diabet fonida taloq bezining gistostruktural va morfofunksional o‘zgarishlarini aniqlash, ularning shakllanish mexanizmlari va oqibatlarini morfologik tahlil qilishga yo‘naltirilgan. Natijalar esa kelajakda qandli diabet bilan kasallangan bemorlar immun holatini baholash, asoratlarni oldini olish va immunokorreksiya usullarini ishlab chiqishda ilmiy asos bo‘lib xizmat qilishi mumkin.

Asosiy qism.

Qandli diabet: metabolik buzilish va umumiy ta’siri

Qandli diabet (diabetes mellitus) — bu glyukoza almashinuvi, insulin ishlab chiqarilishi yoki uning to‘qimalar tomonidan qabul qilinishidagi buzilishlar bilan bog‘liq bo‘lgan surunkali endokrin kasallikdir. Uning I va II turlari mavjud bo‘lib, har ikkisi ham organizmning ko‘plab tizimlariga, xususan, qon-tomir, asab, buyrak, yurak va immun tizimlariga zararli ta’sir ko‘rsatadi. Diabetning uzoq davom etishi organizmda giperglikemiya, dislipidemiya, yallig‘lanish jarayonlarining kuchayishi, oksidlovchi stress va angiopatiyaga olib keladi. Qandli diabet nafaqat energetik almashinuvni, balki immunologik barqarorlikni ham izdan chiqaradi. Shuning uchun bu kasallik nafaqat “metabolik sindrom”, balki “immunologik yetishmovchilik” fonida kechuvchi tizimli holat sifatida qaralmoqda. Ayniqsa, immun tizimining ikkilamchi limfoid organi bo‘lgan taloq bezida kechuvchi gistostruktural o‘zgarishlar ilmiy nuqtai nazardan alohida e’tiborga loyiqdir. Qandli diabet nafaqat energetik almashinuvni, balki immunologik barqarorlikni ham izdan chiqaradi. Shuning uchun bu kasallik nafaqat “metabolik sindrom”, balki “immunologik yetishmovchilik” fonida kechuvchi tizimli holat sifatida qaralmoqda. Ayniqsa, immun tizimining ikkilamchi limfoid organi bo‘lgan taloq bezida kechuvchi gistostruktural o‘zgarishlar ilmiy nuqtai nazardan alohida e’tiborga loyiqdir.

Taloq bezining gistostrukturali va fiziologik roli

Taloq (lien, splen) — immun tizimning eng yirik ikkilamchi limfoid organi hisoblanadi. U qorin bo'shlig'ining chap yuqori kvadrantida joylashgan bo'lib, limfoid to'qimalar, qon ombori va fagotsitar hujayralardan tashkil topgan.

Taloq quyidagi asosiy qismlardan iborat:

Oq pulpa – limfoid tugunchalar, T- va B-limfotsitlar zonasi, periarteriolyar limfoid manzillardan tashkil topgan. Bu qism immun javob shakllanishida ishtirok etadi.

Qizil pulpa – qon bilan to'lgan sinusoidlar, retikuloendotelial hujayralar, makrofaglar va boshqa elementlardan iborat. U eskirgan eritrotsitlarni yo'q qilish, fagotsitoz, plazmada mavjud yot zarrachalarni yo'qotish funksiyalarini bajaradi.

Taloq organizmda ikkita asosiy vazifani bajaradi:

Immunologik vazifa – antigenlarga javob berish, limfotsitlar differensiasiyasi, antitana ishlab chiqarish;

Filtrlovchi (gematologik) vazifa – qon elementlarini tozalash, eskirgan hujayralarni yo'qotish.

Bu a'zo immunitetning markaziy elementi hisoblanib, har qanday tizimli kasallikda, xususan, qandli diabetda, uning strukturaviy, funksional va morfologik holati sezilarli darajada o'zgaradi.

Qandli diabet sharoitida taloq bezining gistostruktural o'zgarishlari.

Ilmiy adabiyotlar tahliliga ko'ra, qandli diabet sharoitida taloq bezida bir qator muhim morfologik o'zgarishlar ro'y beradi. Bu o'zgarishlar giperglikemiya, surunkali yallig'lanish va oksidlovchi stress bilan bevosita bog'liq. Taloqning har ikkala zonasi – oq va qizil pulpa ham ushbu patologik jarayonlardan zararlanadi.

Oq pulpa o'zgarishlari:

Limfoid tugunchalarning hajmi kichrayadi, bu B-limfotsitlar ishlab chiqarilishi va immun javob kuchsizlanishini bildiradi;

Germinativ markazlar zaiflashadi yoki butunlay yo'qoladi, bu immun tizimdagi proliferativ faollikning sustlashganidan darak beradi;

limfotsitlar zonasi siyraklashadi, T-hujayralar soni kamayadi, bu esa hujayraviy immunitetning pasayishiga olib keladi;

Apoptozga uchragan limfotsitlar soni oshadi, bu esa yallig'lanish reaksiyalarining kuchayishiga xizmat qiladi.

Qizil pulpa o'zgarishlari:

Sinusoid kapillyarlarning kengayishi va devorlarining yupqalashuvi kuzatiladi;

Makrofag va retikuloendotelial hujayralarning disfunktsiyasi qayd etiladi, bu fagotsitar faollikni pasaytiradi;

Qon elementlari filtrasiyasi buziladi, eritrotsitlar parchalanishi sekinlashadi;

Sklerotik o'choqlar va gemorragik diapedeslar ko'payadi.

Ushbu gistostruktural o'zgarishlar taloqning normal immun va qon tozalovchi funksiyalarini buzadi. Bu esa diabetik bemorlarda immun yetishmovchilik holatlarini kuchaytiradi.

Morfofunktsional o'zgarishlarning klinik va immunologik oqibatlari.

Taloqdagi gistostruktural buzilishlar klinik jihatdan quyidagilarga olib keladi

Immun tanqislik holatlari – bakterial, virusli va zamburug'li infektsiyalarga nisbatan sezuvchanlik ortadi;

Surunkali yallig'lanishlar – diabetik angiopatiya, nefropatiya va boshqa asoratlarning rivojlanish xavfi ortadi;

Autoimmun reaksiyalar kuchayadi, bu esa diabetga hamroh bo'lgan boshqa autoimmun kasalliklar (masalan, tireoidit, revmatoid artrit) rivojlanish ehtimolini oshiradi;

Oqsil sintezi va immunoglobulinlar ishlab chiqarilishi kamayadi, bu esa zaxiralovchi antitanalar darajasini pasaytiradi;

Qon zaxirasining zaiflashishi – bu taloqdagi eritrotsitlar, trombotsitlar va limfotsitlar resursining buzilishi bilan bog'liq bo'lib, organizmning umumiy gomeostaziga zarar yetkazadi. Shuningdek, retikuloendotelial tizimning faoliyati izdan chiqishi bilan bog'liq immun tanqislik holatlari kuzatilgan. Bu o'zgarishlar klinik amaliyotda bemorlar immun holatini baholashda va immunokorreksiya usullarini ishlab chiqishda muhim rol o'ynaydi.

Taloqdagi o'zgarishlarning molekulyar-biokimyoviy asoslari

Qandli diabetda taloq bezining gistostruktura va funksiyalaridagi o'zgarishlar faqat morfologik darajada emas, balki molekulyar va biokimyoviy bosqichlarda ham yuzaga keladi. Diabet bilan bog'liq surunkali giperglikemiya holatida reaktiv kislorod turlari ning ortiqcha hosil bo'lishi natijasida oksidlovchi stress kuchayadi. Bu esa hujayra membranasi komponentlari, DNK va oqsillarni shikastlaydi. Taloqdagi immun hujayralar (T- va B-limfotsitlar, makrofaglar) ushbu stressga juda sezuvchan bo'lib, ularning proliferatsiyasi va funksional faolligi pasayadi. Shu bilan birga, NF- κ B singari yallig'lanishni faollashtiruvchi transkripsion omillar faollashadi, bu esa proinflamator sitokinlar ishlab chiqarilishini orttiradi.

Ushbu sitokinlar ta'sirida:

Limfoid to'qimalarda atrofiya va degeneratsiya yuzaga keladi;

Taloqdagi sinusoid tomirlar endoteliysi shikastlanadi;

Hujayra o'limi (apoptoz) kuchayadi;

Immun hujayralar migratsiyasi va muvofiqlashtirilgan faolligi buziladi. Bu esa taloqning immunogen javob qaytarish qobiliyatini sezilarli darajada susaytiradi.

Taloqdagi o'zgarishlarning immunologik oqibatlari

Taloq immun tizimining markaziy "monitoring" a'zosi bo'lib, unda antigenlar tan olinadi, zarur limfotsitlar shakllanadi va fagotsitar tozalash jarayonlari amalga oshiriladi. Qandli diabetda bu jarayonlar izdan chiqadi:

Antigen taqdim etuvchi hujayralarning soni kamayadi, bu esa immun javobning boshlanishini kechiktiradi;

T-limfotsitlar va B-limfotsitlar aktivatsiyasi sustlashadi, oqibatda antitana ishlab chiqarilishi kamayadi;

Makrofaglar faoliyati buziladi, bu esa fagotsitoz va infeksiyalarga qarshi kurashni zaiflashtiradi;

Sitotoksik T-hujayralar soni kamayadi, bu esa virusli infeksiyalarni aniqlash va yo'q qilishni qiyinlashtiradi;

Taloqning immun nazorati susayadi, bu esa avtoimmun va yallig'lanishli kasalliklarning kuchayishiga olib keladi.

Ko'plab klinik kuzatuvlarda qandli diabetli bemorlarning bakterial va virusli infeksiyalarga nisbatan chidamliligi pastligi aniqlangan bo'lib, buni aynan taloqdagi immun va morfologik buzilishlar bilan izohlash mumkin.

Diabet fonida taloqdagi angionevrotik va degenerativ jarayonlar Qandli diabetning yana bir muhim ta'siri — angiopatiya, ya'ni kichik qon tomirlarning buzilishi orqali amalga oshadi. Taloq tomirlarining devorlari ingichka va sezuvchan bo'lgani sababli, diabet sharoitida:

Kapillyar va venula devorlari qalinlashadi, bu esa perfuziya yetishmovchiligiga olib keladi.

Sinusoidal tomirlar kengayadi, ba'zi joylarda mikroanevrizma va diapedetik qon quyilishlar yuzaga keladi;

Taloqning nerv elementlarida degeneratsiya boshlanadi, bu esa vegetativ regulyatsiya buzilishiga sabab bo'ladi;

Fibrozo va skleroz o'choqlari paydo bo'ladi, bu esa to'qimaning funksional qismini almashtiradi.

Yuqoridagi jarayonlar taloqni nafaqat immun, balki gematologik jihatdan ham nafaqat a'zoga aylantirib qo'yadi. Oqsil sintezi, hujayra regeneratsiyasi va filtratsion faollikning izdan chiqishi organizmning umumiy holatiga salbiy ta'sir ko'rsatadi.

Qandli diabet va taloq: klinik jihatdan amaliy ahamiyati

Taloqdagi o'zgarishlar ko'p hollarda klinik jihatdan yashirin kechadi. Ammo diabetga chalingan bemorlarda ushbu o'zgarishlar kuzatiladi:

Surunkali bronxit va pnevmoniyalarning ko'payishi;

Yara va nekrotik jarayonlarning uzoq bitmasligi;

Virusli infeksiyalarning uzoq davom etishi;

Revmatik yoki avtoimmun sindromlar;

Shuningdek, limfotsitoz, limfopeniya, trombositopeniya kabi laborator ko'rsatkichlar bevosita taloqdagi strukturaviy va funksional buzilishlar bilan bog'liq bo'ladi. Shu bois, diabetik bemorlarning umumiy ahvolini baholashda taloq bezining strukturalari va faoliyatiga e'tibor qaratish, zamonaviy diagnostik vositalar yordamida u yerda kechayotgan o'zgarishlarni erta aniqlash muhim klinik ahamiyatga egadir.

Xulosa. Qandli diabet organizmning barcha hayotiy tizimlariga, jumladan, immun tizimining asosiy a'zolaridan biri bo'lgan taloq beziga ham salbiy ta'sir ko'rsatadi. Diabet sharoitida rivojlanadigan surunkali giperglikemiya, oksidlovchi stress, mikroangiopatiya va yallig'lanish reaksiyalarining kuchayishi taloq to'qimalarida chuqur morfologik va funksional o'zgarishlarga olib keladi. Ushbu o'zgarishlar natijasida taloqning asosiy vazifalari — immunologik himoya, antigenlarga javob shakllantirish va fagotsitar tozalash jiddiy darajada izdan chiqadi. Diabet bilan bog'liq bu kabi o'zgarishlar bemorlarda infeksiyon kasalliklarga nisbatan sezuvchanlikni oshiradi, immun yetishmovchilik holatlari va surunkali yallig'lanish jarayonlarini kuchaytiradi. Shu bois, qandli diabet kasalligini kompleks yondashuv asosida davolashda taloq bezining gistostruktura va funksional holatini o'rganish va nazorat qilish muhim amaliy ahamiyat kasb etadi.

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AGRAR SOHA KORXONALARI FAOLIYATINI RIVOJLANTIRISHDA
DIVERSIFIKATSIYALASH STRATEGIYASI

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Аннотация: Мақолада агросаноат корхоналари фаолияти самарадорлиги ошириш омили сифатида ишлаб чиқаришни диверсификациялаш масалалари кўриб чиқилган. Агросаноат корхоналарида диверсификациялашнинг ўзига хос жиҳатлари асослаб берилган, ҳамда қишлоқ хўжалик корхоналари фаолиятини диверсификациялаш стратегиясининг асосий йўналишлари шакллантирилган.

Калит сўзлар: диверсификация, қишлоқ хўжалиги, стратегия, бошқарув, интеграциялаштириш салоҳияти, интеграциялашувни ривожлантириш йўналишлари, интеграциялаштириш модели.

Аннотация: В статье рассмотрены вопросы диверсификации производства, как фактор повышения эффективности предприятий аграрной промышленности. Обоснованы специфические аспекты диверсификации на предприятиях аграрной промышленности и сформированы основные направления стратегии диверсификации предприятий сельского хозяйства.

Ключевые слова: диверсификация, сельское хозяйство, стратегия, управление, потенциал интеграции, направления развития интеграции, модель интеграции.

Annotation: Considered the issues related to the divestment as a process of increasing the economic efficiency of enterprises. Features of diversification in agricultural production. Formulated alternative strategies of diversification of agricultural enterprises.

Keywords: a diversification, agriculture, strategy, management, economic efficiency. integration potential; directions of development integration; integration model.

Respublikamiz agrar sohasida amalga oshirilayotgan iqtisodiy islohotlarning bugungi bosqichidagi muhim xususiyatlaridan biri – sohaga ilmiy sig‘imi yuqori bo‘lgan, resurstejamkor, innovatsion g‘oya va fan yutuqlariga asoslangan ishlab chiqarishning kirib kelishi hisoblanadi.

Bu o‘z navbatida milliy iqtisodiyotimiz barqarorligini ta’minlashga xizmat qiladigan

agrar soha tarmoq tuzilishini shakllantirishi bilan birga, sohadagi xo‘jalik yurituvchi subyektlar o‘rtasida raqobatni kuchaytirib, ularning nafaqat ichki bozorlarda balki tashqi bozorlarda ham raqobatbardosh bo‘lishini ta’minlamoqda.

Darhaqiqat, mahsulot va resurslar bozorida raqobat kuchaygan sari aksariyat qishloq xo‘jalik korxonalari uchun qishloq xo‘jalik mahsulotlari ishlab chiqarishni takomillashtirish, qayta ishlash korxonalari ehtiyojidan kelib chiqqan holda, assortiment hamda qishloq xo‘jalik mahsulotlari bozori konyukturasini kengaytirishning ahamiyati ortib boradi. Bu o‘z navbatida, istiqbolda qishloq xo‘jalik mahsulotlarini yetkazib beruvchilar va qayta ishlash korxonalarining o‘zaro birgalikdagi faoliyatini olib borish hamda hamkorlikni amalga oshirishning yangi samarali mexanizmini ishlab chiqish va uni joriy etishni zaruriyatga aylantiradi.

Bunday sharoitda xo‘jalik subyektlari xo‘jalikni uzluksiz rivojlanishni ta’minlash maqsadida, bir tomondan o‘zlarining uzoq muddatli strategik rejalarini tuzib olishlari lozim bo‘lsa, ikkinchi tomondan, esa ular korxonadagi mavjud ishlab chiqarish ixtisoslashuviga muqobil yo‘llarni izlashlari kerak bo‘ladi. Istiqbolli rejalashtirishning strategik muqobillaridan biri diversifikatsiya hisoblanadi.

Ishlab chiqarishni diversifikatsiyalash – bu korxonada ishlab chiqarilayotgan mahsulotlar assortimentini kengaytirish, mahsulot turini o‘zgartirish, ishlab chiqarish samaradorligini oshirish, iqtisodiy jihatdan foydaga erishish, inqirozning oldini olish maqsadida ishlab chiqarishning yangi turlarini o‘zlashtirishdir.

Ishlab chiqarishni diversifikatsiyalash ko‘pincha mahsulot va xizmatlar sifatining oshirilishiga olib keladi. Chunki, ishlab chiqaruvchining mahsulot yangi turlarini o‘zlashtirish bilan bir qatorda ularning iste’mol xususiyatlarini yaxshilashga intilishi pirovardida, sifat darajasining o‘shirishini ta’minlaydi. Bu esa, mazkur mahsulotni sotish hajmining ko‘payishi bilan birga ularni sotish bozorlarining kengayishiga ta’sir ko‘rsatadi[1].

Diversifikatsiya bir turdagi mahsulotni ommaviy ishlab chiqarish samarasini, turli mahsulotlar ishlab chiqarish orqali o‘shirish strategiyasini amalga oshirish hisobiga siqib chiqardi. Turli mahsulotlar ishlab chiqarish samarasining mohiyati shundaki, ko‘p turdagi mahsulotlarni bitta yirik korxonada ishlab chiqarishga nisbatan shu turdagi mahsulotlarni katta bo‘lmagan ixtisoslashgan korxonalarda ishlab chiqarish foydaliroqdir.

Diversifikatsiyalashning asosiy maqsadi bir nechta tarmoqda faoliyat olib borish hisobiga foydani oshirish hamda risk darajasini kamaytirish hisoblanadi. Diversifikatsiyalashgan korxonalar raqobat kurashida barqarorroq bo‘lib, ularda konyuktura, tuzilmaviy hamda sikl o‘zgarishlari hisobiga yuzaga keladigan risk darajasi pastroq bo‘ladi.

Diversifikatsiyalash xo‘jalik subyektlarini rivojlantirishning umumqabul qilingan zaruriy usullaridan hisoblanadi.

Bugungi kunda, qishloq xo‘jalik mahsulotlarini ishlab chiqaruvchilar bilan ushbu mahsulotlarni qayta ishlovchilar o‘rtasidagi faoliyatni yo‘lga qo‘yishning yangi mexanizmlarini yaratish zaruriyati, mavjud ishlab chiqarishni optimallashtirish va

qayta ishlash korxonalari talablaridan kelib chiqqan holda, yangi ishlab chiqarishlarni joriy etish zaruriyati bilan uyg'unlashib borayotganligi bois, agrar soha korxonalarini diversifikatsiyalashning dolzarbligi yanada ortib bormoqda.

Fikrimizcha, agrar sohada diversifikatsiyalash dasturiy tadbirlarini shakllantirish va amalga oshirish to'g'risida qaror qabul qilishda, qishloq xo'jaligining o'ziga xos xususiyat va jihatlarini e'tiborga olish maqsadga muvofiq:

- ishlab chiqarishning mavsumiylik xarakterdaligi;
- biologik va iqtisodiy jarayonlarning qo'shilib ketishi;
- yerning ishlab chiqarish vositasi sifatida qaralishi va boshqalar.

Aynan, mana shu o'ziga xoslik qishloq xo'jaligi korxonalarining ish faoliyati natijalari va uning iqtisodiy samaradorligiga ko'p jihatdan bog'liqdir.

Ishlab chiqarishni diversifikatsiyalash jarayoni uzoq muddatli istiqbolda korxonaning iqtisodiy va moliyaviy jihatdan yuksalishiga olib kelsada, ahamiyatli darajadagi sarf-xarajatlarni taqozo etishi sababli joriy natijalarga sezilarli ta'sir ko'rsatishi mumkin. Bu esa korxona faoliyati bilan bog'liq bo'lgan turli iqtisodiy subyektlarning manfaatlariga ham turlicha ta'sir ko'rsatadi[1].

Tadqiqotlar ko'rsatishicha, bugungi kunda integratsiyalashgan tizimlarni shakllantirish, ular faoliyatini tashkil etish va rivojlantirishga quyidagi omillar to'sqinlik qilmoqda:

- qishloq xo'jaligiga nisbatan qayta ishlash sanoatida ijtimoiy mehnat unumdorligi darajasining birmuncha yuqori darajada ekanligi;
- agrosanoat majmuiga kiruvchi aksariyat korxonalarda integratsiyalashgan tuzilmalarni yaratishga bo'lgan manfaatdorlikning birmuncha sust rivojlanayotganligi;
- integratsiyalashgan tuzilmalarni shakllantirish va ular faoliyatini tashkil etish sohasida huquqiy bazaning takomillashmaganligi;
- tarmoqning va hududning o'ziga xos tomonlarini hisobga olgan holda, agrosanoat integratsiyasi shaklini tanlashga imkon beradigan ilmiy asoslangan uslubiyotni takomillashtirishga bo'lgan zaruriyat;
- agrosanoat majmuasi korxonalari moliyaviy holatining qoniqarli darajada emasligi va ko'pchilik qishloq xo'jalik tashkilotlarining to'lov qobiliyatining korxonada kengaytirilgan takror ishlab chiqarishni amalga oshirish uchun moliyaviy imkoniyatlarining cheklanganligi;
- qishloq xo'jalik va qayta ishlash korxonalari moddiy-texnikaviy salohiyatining pastligi boshqalar.

Ishlab chiqarishni diversifikatsiyalash iqtisodiy samaradorligini hisoblashda quyidagilarni e'tiborga olish zarur:

- divesifikatsiya natijasida olingan qo'shimcha daromad;

- ishlab chiqarishni diversifikatsiyalash hisobigan mahsulot bozoridagi infohratuzilma xizmatlaridan foydalanish imkoniyatining oshganligi;
- xizmatlardan foydalanish ko'lamining oshganligi va tovar mahsulot sotish hajmining oshganligi bois, xarajatlarning qisqarishi, tannarxining pasayishi;
- yangi mahsulot ishlab chiqarishni o'zlashtirilishi va bunga mos ravishda innovatsion texnologiyalarning kirib kelishining kuchayishi va boshqalar;

Diversifikatsiyalash strategiyasini qo'llash har doim ham qishloq xo'jaligi korxonalariga muvaffaqiyat keltirmaydi, shu boisdan ham rahbariyat doimiy ravishda uni qo'llashning oqibatlarini tahlil qilib borishi, agar faoliyat samarasiz bo'lsa, faoliyat yo'nalishiga tegishli o'zgartirishlar kiritishi kerak.

Bunday holatda rivojlangan mamlakatlar tajribasiga asoslanib, quyidagi muqobil strategiyalar taklif etilishi mumkin:

- yangi tarmoqlarda mavqega ega bo'lish yoki diversifikatsiyalashgan faoliyat yo'nalishlaridagi mavqeni mustahkamlash maqsadida boshqa tarmoqlarga kirib borish yoki yangi vositalarga egalik qilish;
- korxonaning iqtisodiy strategiyasiga javob bermayotgan faoliyat yo'nalishlaridan voz kechish;
- diversifikatsiya bazasini qisqartirish, jumladan, kuchsiz yo'nalishlarni yo'q qilish yo'li bilan;
- samaradolik darajasi past bo'lgan, foyda keltirmayotgan, shuningdek, zarar keltirayotgan bo'linmalar faoliyatini to'xtatish hamda ishlab chiqarish yo'nalishlarini yopish[2].

Xulosa qiladigan bo'lsak, qishloq xo'jalik korxonalari faoliyatini diversifikatsiyalash strategiyasini tanlash ularning ichki hamda tashqi iqtisodiy muhiti salohiyati bilan aniqlanadi. Qishloq xo'jalik korxonalari faoliyatini diversifikatsiyalash strategiyasini tanlashning tashkiliy – iqtisodiy mexanizmi o'z ichiga strategik ko'ra bilishlikni, uning ichki va tashqi muammolarini tarkiblashni, missiyasi va maqsadlarini shakllantirishni, strategik tahlil qilishni, strategik muqobillarni aniqlashni, strategiyani tanlashni, uning bajarilishi ustidan nazorat o'rnatishni hamda samaradorligini aniqlashni o'z ichiga oladi.

Yuqorida bildirilgan uslubiy yondashuv va amaliy tavsiyalarni amaliyotga qo'llash respublikamiz agrar soha va tarmoqlari korxonalari samaradorligini diversifikatsiyalash strategiyasi asosida oshirishni ta'minlashga xizmat qiladi.

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“PSIHO-ENDOKRINOLOGIK O‘ZGARISHLARNING O‘SMIRLAR RUHIY SALOMATLIGIGA TASIRI”

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ANNOTATSIYA: Maqolada o‘smirlik (pubertat) davrida endokrin tizimda kechuvchi gormonal o‘zgarishlarning o‘smirlar ruhiy salomatligiga ta’siri ilmiy tahlil qilindi. Gormonlarning — xususan estrogen, testosteron, kortizol, dopamin va serotonin darajalarining — kayfiyat, o‘zini baholash va ijtimoiy xulqqa ta’siri ko‘rib chiqiladi. Tadqiqotda o‘smirlik davrida kuzatiladigan psixologik beqarorlik, stressga moyillik, o‘z tanasini qabul qilmaslik kabi holatlar gormonal o‘zgarishlar bilan uzviy bog‘liqligi yoritilgan. Maqolada psixo-endokrinologik yondashuvning pediatriya amaliyotidagi ahamiyati va o‘smirlar bilan ishlovchi mutaxassislar uchun amaliy tavsiyalar keltiriladi.

KALIT SO‘ZLAR: pubertat, gormonlar, psixo-endokrinologiya, o‘smirlik davri, ruhiy salomatlik, stress, o‘zini baholash.

O‘smirlik (pubertat) davri inson hayotidagi eng murakkab fiziologik va psixologik bosqichlardan biridir. Bu davrda endokrin tizimning faoliyati kuchayib, jinsiy bezlar, gipofiz va gipotalamus o‘rtasidagi gormonal muvofiqlashuv tizimi faol ishlay boshlaydi. Ushbu jarayon natijasida estrogen, testosteron, kortizol, dopamin va serotonin kabi biologik faol moddalar darajasi o‘zgaradi. Aynan shu gormonlar o‘smirning nafaqat jismoniy rivojlanishida, balki uning hissiy holati, kayfiyati, o‘zini baholashi va ijtimoiy xulqida ham muhim rol o‘ynaydi. Pubertat davri o‘smirning o‘zini kashf etish, shaxsiy “men”ini shakllantirish va ijtimoiy muhitda o‘rnini topish jarayoni bilan kechadi. Shu sababli gormonal o‘zgarishlar bilan bir paytda kechuvchi psixologik beqarorlik — tabiiy, ammo nozik holatdir. Agar bu jarayon nazoratdan chiqsa yoki tashqi omillar (stress, oilaviy muhit, ijtimoiy bosim) bilan kuchaysa, ruhiy salomatlik buzilishlariga olib kelishi mumkin. Shu nuqtai nazardan, psixo-endokrinologik tahlil o‘smirlik davrini chuqurroq tushunish uchun muhim ilmiy yondashuv hisoblanadi.

Pubertat jarayonida gormonlar markaziy asab tizimining faoliyatiga bevosita ta’sir ko‘rsatadi. Gormonlar va neyrotransmitterlar o‘rtasida kuchli o‘zaro aloqadorlik mavjud: masalan, testosteron va estrogen miqdorining o‘zgarishi serotonin va dopamin almashinuvi bilan chambarchas bog‘liq. Bu esa o‘smirning kayfiyat barqarorligi, moti-

vatsiyasi va o'zini baholash darajasiga bevosita ta'sir qiladi.

Estrogen qizlarda hissiy barqarorlik va empatiya bilan bog'liq bo'lsa-da, uning keskin ko'tarilishi yoki pasayishi tez-tez kayfiyat o'zgarishlari, yig'loqilik, o'ziga ishonchsizlik va tashvish hissini keltirib chiqarishi mumkin. Shu bilan birga, estrogen miyada serotonin ishlab chiqilishini rag'batlantiradi, bu esa qisqa muddatli eforiya, ammo uzoq muddatda hissiy charchoqqa olib kelishi mumkin.

Testosteron o'g'il bolalarda mustaqillik hissi, o'zini himoya qilish instinkti va raqobatga moyillikni oshiradi. Biroq bu gormonning haddan tashqari ko'payishi agressivlik, impulsiv xatti-harakat va konfliktlarga moyillikni kuchaytiradi. Aksincha, testosteron darajasining pastligi o'smirda o'ziga ishonchsizlik, ijtimoiy chekinish va depressiv holatlarni yuzaga keltiradi.

Kortizol – stress gormoni sifatida tanilgan bo'lib, o'smirlik davrida uning o'zgarishlari ayniqsa sezilarli. Haddan ortiq kortizol darajasi uyqusizlik, diqqat susayishi va hissiy toliqish holatini chaqiradi. Agar o'smirda ijtimoiy qo'rquv yoki oilaviy ziddiyatlar mavjud bo'lsa, kortizol sekretsiyasi ortib, bu ruhiy beqarorlikni kuchaytiradi.

Dopamin va serotonin — “baxt gormonlari” sifatida tanilgan neyrotransmitterlar — o'smirlik davrida motivatsiya, ijtimoiy faollik va o'zini qabul qilish hissini boshqaradi. Biroq gormonal o'zgarishlar davrida ularning muvozanati buzilishi, o'smirda hissiy keskinlik, sababsiz xavotir yoki tez charchash kabi holatlarni keltirib chiqaradi. Bu jarayonlarning barchasi psixo-endokrin muvozanat tushunchasini yuzaga keltiradi. Ya'ni, gormonlar va ruhiy holat o'rtasidagi o'zaro ta'sir ikki tomonlama kechadi: gormonlar psixologik holatni o'zgartirsa, stress va hissiy bosim ham gormonal faoliyatga ta'sir ko'rsatadi. Masalan, o'smirlikda uzoq davom etgan psixologik stress gipotalamus-gipofiz-buyrak usti o'qi faoliyatini buzib, kortizol ishlab chiqilishini oshiradi; bu esa, o'z navbatida, immun tizim va asab tizimining muvozanatini buzadi. Ijtimoiy muhit ham bu jarayonlarda muhim o'rin tutadi. Bugungi kunda o'smirlar o'z tengdoshlari bilan ijtimoiy tarmoqlarda taqqoslanadi, ideal tashqi ko'rinish me'yorlariga mos kelmaslik ularda psixologik noqulaylik tug'diradi. Ayniqsa, qizlarda estrogenning o'zgaruvchanligi fonida o'z tanasidan qoniqmaslik kuchayadi, bu esa o'zini past baholash va depressiyaga moyillikni oshiradi. Shu bois, pubertat davrida ruhiy salomatlikni qo'llab-quvvatlash faqat psixologik yondashuv bilan emas, balki endokrin mexanizmlarni ham inobatga olgan holda amalga oshirilishi zarur. Shifokor, psixolog va ota-ona hamkorligida o'smirning fiziologik o'zgarishlariga mos psixologik yordam ko'rsatilsa, bu jarayon tabiiy, og'riqsiz va barqaror kechadi.

Xulosa qilib aytganda, Pubertat davri — bu faqat fiziologik o'zgarishlar bosqichi emas, balki inson ruhiyati, o'zini anglash va shaxs sifatida shakllanish davridir. Aynan shu paytda gormonal muvozanatdagi eng kichik o'zgarish ham o'smirning hissiy holati, fikrlashi va xulqida sezilarli aks etadi. Shu sababli bu davrni to'g'ri tushunish,

o‘smirni faqat “kayfiyati o‘zgaruvchan” deb baholamasdan, balki undagi har bir hissiy tebranish ortida fiziologik mexanizmlar borligini anglash juda muhimdir. Tadqiqotlar shuni ko‘rsatadiki, endokrin tizimdagi har bir o‘zgarish ruhiy salomatlikka bevosita ta’sir qiladi. Estrogen va testosteronning notekis sekretsiyasi, kortizolning ortishi yoki dopaminning pasayishi — bularning barchasi o‘smir kayfiyati, o‘zini baholashi va hayotga qarashiga ta’sir etuvchi asosiy omillardir. Demak, ruhiy barqarorlik — bu na faqat psixologik, balki fiziologik muvozanatni ham talab qiladigan holatdir. Bugungi kunda tibbiyot shunchaki kasallikni davolash bilan cheklanmasligi, balki insonning ruhiy va gormonal uyg‘unligini ta’minlashga ham e’tibor qaratishi kerak. Chunki har bir o‘smir — bu kelajakdagi yetuk shaxs, va u sog‘lom, barqaror psixika bilan voyaga yetishi uchun tibbiy, ijtimoiy va oilaviy qo‘llab-quvvatlov zarur.

Menimcha, eng muhim narsa — bu davrni “muammo” deb emas, balki inson rivojlanishidagi tabiiy bosqich deb qabul qilishdir. To‘g‘ri yondashuv, sabr va tushunish orqali o‘smir o‘zini anglashni, his-tuyg‘ularini boshqarishni o‘rganadi. Va aynan shunda pubertat davridagi gormonal o‘zgarishlar insonning yetuk, mustahkam va ruhiy jihatdan sog‘lom shaxsga aylanishida poydevor vazifasini bajaradi.

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PEDIATRIYADA SUN'İY INTELEKTNING DOLZARBLIGI**Xudoyberdiyeva Rayhona Abbos qizi****Toshkent Davlat Tibbiyot Universiteti****Annotatsiya:**

Ushbu maqolada pediatriyada sun'iy intellektning (SI) roli va ahamiyati keng tahlil qilinadi. Tadqiqotlarda SI turlari (Mashinalarni o'rganish, Chuqur o'rganish, Kompyuter ko'rish, NLP va chat-botlar) va ularning bolalar sog'lig'ini saqlashdagi amaliy qo'llanilishi misollar bilan keltirilgan. Shuningdek, maqolada SI afzalliklari, kamchiliklari, O'zbekistonda pediatriyada joriy etilishi va xorijiy mamlakatlar bilan taqqoslash ko'rib chiqilgan.

Kalit so'zlar: Sun'iy intellekt, pediatriya, mashinalarni o'rganish, chuqur o'rganish, kompyuter ko'rish, NLP, chat-bot, diagnostika, O'zbekiston, xorijiy tajriba.

Annotation

This article provides a comprehensive analysis of the role and significance of artificial intelligence (AI) in pediatrics. The study presents examples of AI types (Machine Learning, Deep Learning, Computer Vision, NLP, and chatbots) and their practical applications in child healthcare. Furthermore, the article examines the advantages and limitations of AI, its implementation in Uzbekistan, and compares it with international practices.

Keywords: Artificial Intelligence, Pediatrics, Machine Learning, Deep Learning, Computer Vision, NLP, Chatbot, Diagnosis, Uzbekistan, International Experience.

Аннотация:

В данной статье проводится всесторонний анализ роли и значимости искусственного интеллекта (ИИ) в педиатрии. Приведены примеры типов ИИ (машинное обучение, глубокое обучение, компьютерное зрение, обработка естественного языка и чат-боты) и их практическое применение в детском здравоохранении. Также рассматриваются преимущества и ограничения ИИ, его внедрение в Узбекистане и сравнение с международным опытом.

Ключевые слова: Искусственный интеллект, педиатрия, машинное обучение, глубокое обучение, компьютерное зрение, обработка естественного языка, чат-бот, диагностика, Узбекистан, международный опыт.

So'nggi yillarda sun'iy intellekt (SI) tibbiyotning eng muhim texnologik yo'nalishlaridan biriga aylandi. U dastlab tasvirlarni tahlil qilish va tadqiqotlarda qo'llanilgan bo'lsa, hozirda diagnostika, davolash jarayonlarini optimallashtirish, individual terapiya rejalashtirish va pediatriyada profilaktik choralarni ishlab chiqishda keng qo'llanilmoqda. Jahon sog'liqni saqlash tashkiloti (WHO, 2023) ma'lumotlariga ko'ra, SI texnologiyalari yordamida diagnostik aniqlik 25–40% ga oshgan, bu ayniqsa bolalar tibbiyotida muhimdir. Tibbiyotdagi sun'iy intellektning umumiy roli haqida ingliz tadqiqotchilari (Hinton & LeCun, 2022; Stanford Medicine AI Initiative, 2023) ta'kidlaganidek, quyidagi asosiy ustunliklari bor:

Klinik tasvirlarni tahlil qilishda inson xatosini kamaytirish.

Kasalliklarning erta bosqichini aniqlash.

Individual terapiya rejalarini ishlab chiqish.

Telemeditsina va masofaviy diagnostika imkoniyatlarini yaratish.

Masalan, Johns Hopkins Medicine (2023) tadqiqotida yurak yetishmovchiligi va diabetni erta aniqlash algoritmi 92% aniqlik ko'rsatgan. Cambridge University Medical AI Lab (2022) esa pediatriyada o'pka va yurak kasalliklarini aniqlashda SI modelining inson shifokoriga nisbatan 18% samaraliroq ishlashini ko'rsatgan.

Pediatriya — bolalar organizmining o'ziga xosligi sababli murakkab soha. Shu bois SI tizimlari quyidagicha yordam beradi:

Harvard Medical School (2023): SI algoritmlari chaqaloqlarda pnevmoniyani aniqlashni 3 soniyada bajaradi, shifokor uchun esa bu jarayon 15 daqiqa davom etadi.

Boston Children's Hospital (2024): SI yordamida 3 yoshgacha bo'lgan bolalarda autizm spektr buzilishlarini 89% aniqlik bilan tashxis qilish imkoniyati yaratilgan.

German Pediatric AI Consortium (Berlin, 2023): KinderMedAI tizimi 12 ming bolalarning rentgen va MRI tasvirlari asosida o'pka kasalliklarini 96% aniqlik bilan aniqlaydi. Bular biz kuzatgan statistikaning bir qismi.

Sun'iy intellektning quyidagi turlarini biz Pediatriyada qo'llasak bo'ladi:

1. Mashinalarni o'rganish (Machine Learning, ML): bolalarda kasallik xavfini bashorat qilish.
2. Chuqur o'rganish (Deep Learning, DL): tasvir va laborator natijalarni tahlil qilish.
3. Kompyuter ko'rish (Computer Vision, CV): ultratovush, rentgen va MRI tasvirlarini tahlil qilish.
4. Ovozli diagnostika tizimlari (Speech Recognition AI): bolalarning nafas va yurak

tovushlarini analiz qilish.

5. Tabiiy tilni qayta ishlash (Natural Language Processing, NLP) va chat-botlar: pediatrik maslahat va kuzatuv.

Ammo shuni ham aytish joizki, uning afzalliklari bilan bir qatorda kamchiliklari ham bor. Masalan, ma'lumot yetishmasligi, mutaxassislarni tayyorlash zarurati, huquqiy va axborot xavfsizligi masalalari, yuqori xarajatlar va texnologik baza talab etilishi va boshqalar. Bugungi kunda O'zbekistonda pediatriya sohasida SI tizimlari faqat sinov bosqichida turibdi. Yaqin kelajakda biz ham bu tizimli rejaga o'tish arafasida turibmiz va bu bo'yicha bir qancha loyihalarimiz bor.

Toshkent tibbiyot akademiyasida telemeditsina va laborator natijalarni avtomatik tahlil qiluvchi pilot loyihalar mavjud.

Xorijiy mamlakatlar bilan taqqoslaydigan bo'lsak, AQSHda telemeditsina va avtomatlashtirilgan pediatrik diagnostika tizimlari keng qo'llaniladi. Germaniyda KinderCare-AI platformasi bronxit, anemiya va genetik kasalliklarni avtomatik tahlil qiladi. Rossiya davlatida "MedAI" loyihasi diagnostika xatolarini 23% ga kamaytirganini ko'rishimiz mumkin.

Xulosa qilib aytganda sun'iy intellekt tashxis qo'yishda aniqlikni oshiradi, vaqtini tejaydi va shifokorga qaror qabul qilishda yordam beradi. Biroq shuni alohida ta'kidlash lozimki, sun'iy intellekt hech qachon inson — shifokorning o'rnini to'liq bosa olmaydi. Chunki har bir bemor, ayniqsa bola, faqat raqamlar va algoritmlar orqali emas, balki hissiyot, empatiya va insoniy kuzatuv orqali to'liq baholanadi. Shifokor birinchi navbatda bemorni obyektiv tekshiradi, suhbatlashadi, tana tilini, his-tuyg'ularini, o'ziga xos fiziologik javoblarini tahlil qiladi. Bu esa hozircha hech bir algoritim to'liq bajara olmaydigan insoniy fazilatdir. Shu bois SI — bu yordamchi vosita, ammo asosiy qaror va mas'uliyat shifokorga tegishlidir.

Kelajakda tibbiyotda inson va sun'iy intellektning uyg'un hamkorligi — eng to'g'ri yo'ldir. Tibbiyotning maqsadi texnologiyani mutlaq markazga qo'yish emas, balki inson hayotini saqlash va yaxshilashdir.

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