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ROLE OF OXIDATIVE STRESS IN THE OCCURRENCE OF THE LEGG-CALVE-PERTHES DISEASE.**BASIC CONCEPTS OF PATHOGENESIS, DIAGNOSIS AND TREATMENT**

(literature review)

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In article the authors consider a modern level of knowledge of etiology, pathogenesis of the disease Legg-Calve-Perthes (DLCP), a new approach to diagnosis and treatment DLCP in view of knowledge about of oxidative stress, antioxidant system, lipid peroxidation.

Key words: disease Legg-Calve-Perthes, oxidative stress, antioxidant system, lipid peroxidation.

The Disease Legg-Calve-Perthes (DLCP) is a complex pathological process in the hip joint, which is based on ischemic disorders, leading to the aseptic necrosis of the femoral head, and the outcome is a disruption of the normal anatomical structure and function the joint.[5]

Questions of etiology and pathogenesis of the disease to date remain open.[19]

In the development of the disease Legg-Calve-Perthes (DLCP) plays a crucial role oxidative stress and the decrease in the protective functions of the antioxidant system (AOS).[23] The doctrine of innervation receptacles closely connected with the problem of the trophic action of the nervous system, particularly sympathetic.[11]. Under the influence of multiple factors (stress, cold, trauma) and the presence of background changes (neyrodisplaziya, vazodisplaziya, osteodisplaziya) [18, 20] there is an activation of sympathetic nervous system and the release of norepinephrine in the blood stream [20].

Underdevelopment of microvascular network and its terminal departments leads to the fact that it could not compensate for the critical state in hemodynamics joint. [15] Appearance in

the blood of excessive amounts of noradrenaline indirectly, through the release of calcium and fatty acids, can stimulate the intensity of free oxidation in the mitochondria and, thereby, lead to an increase in oxygen consumption and heat production. [22]

Thus identified with the help of additional methods of research violation of the hips, not stacked in frameworks gipovaskulyarization purely vasodistodisplastics genesis, associated with disorders relation between neurodynamic regulation of the hip joint tissues, including microcirculation vascular bed. [15] The greatest role of these disorders is at the early stages of the disease, affecting the transfer of the convertible vascular disorders in the stage of decompensation of microcirculation in bone and cartilage development and necrotic parts. [11]

Articular tissue is very sensitive to the effects of internal and external factors, under the influence of which may cause spasm or thrombosis subchondral area of the bone or the synovial membrane with the subsequent disturbance of microcirculation and the development of oxygen insufficiency in the cartilage [15]. In the tissues of the elements of the joint is the accumulation of oxidized products of metabolism. Malnutrition cartilage leads to its destruction. [7,22]

Thus, DLCP take place neurological, cardiovascular and metabolic disorders (neurohumoral character). It is not only variation vessels bringing blood the hip joint, the blood flow and circulation, but also rolling and rheological properties of blood. [1,19] Biogenic changes in the vessels of the hip joint, the ends of venous blockade with subsequent venous hypertension. [19] Some researchers confirm that change in the rheological properties of blood is one of the leading mechanisms of DLCP, others believe this is a consequence of the neuroendocrine changes that occur as a result of the haemostaziological and rheological factors. [1] There is also evidence, that in the mechanism of development of DLCP an important role is played by the processes of lipid peroxidation (LPO) and antioxidant system (AOS). [14]

Therefore, the emerging pathology is also the result of oxidative stress and reduce the protective functions of the AOS. [2]

It is known that the acceleration of the processes of lipid peroxidation (POL) is one of the reasons for destabilization of the membranes and the development of pathological changes [9]. Danger to the body of LPO products represent only in the case of disturbances in the functioning of the AOS or the depletion of its reserve capacities. It is known, that the system antiperoxidant protection consists of enzymatic and nonenzymatic links. The enzymatic system includes several enzymes, superoxide dismutase, catalase, glutathionperoxidase, glutathionreductase, glutathione-s-transferase and ceruloplasmin. Many of them catalyze reactions, as a result of which toxic free radicals and peroxide neutralized [14].

Acceleration of the processes of peroxidation is one of the reasons for destabilization of the membranes and the development of pathology [9]. At the first stage of the process are formed diene conjugates fatty acids (DC FA). From the formed DC FA with further impact on them hydroxyl radicals are formed lipids of peroxidation. The products of the peroxidation cause conformational changes in the phospholipids and complex of phospholipids, which leads to the disruption of the organelles of cells, organs and the whole organism. In the field of action of peroxide radicals fatty acids are broken into fragments, at the ends of which are located aldehyde groups, possessing high reaction ability. If the reaction occurred with the two parties, formed malondialdehyde (MDA). Reacting to SH and CH₃-groups of proteins, MDA inhibits the activity of enzymes: cytochrome oxidase, hydroxylase and etc. Thus, peroxidation has an essential role in the regulation of the metabolism of membrane lipids, changing the physico-chemical properties and permeability of biological membranes in physiological conditions. [9].

Group of substances possessing ability to inhibit the formation of peroxides classified in the group of antioxidants.[2, 5] Some of them is a derivative heterocyclic compounds pyrimidine derivatives. It was found that pyrimidine derivatives in particular, the drug of choice, in our case, mexidol, increase the resistance of the organism to a variety of adverse effects, effect on the neurological, cardiovascular and metabolic link of the DLCP. [5, 14]

In our opinion, in all existing conservative treatment methods DLCP there is no method of therapy that can influence on the pathogenic processes in the tissues of the joints, to prevent the transition to the irreversible stage necrotic parts of the femoral head and enhance the effectiveness of treatment by preventing the expansion volume neurodystrophic tissue and vascular reactions. [11,19] We believe that antioxidant therapy may be used in a specific pathogenetic method in combined treatment of DLCP. [14]

Existing methods of diagnostics allow to confirm our findings and to make treatment of reasonable and purposeful. [2, 3, 6, 21]

For the diagnosis DLCP, in our work, we have used: x-rays of the hip joints, computed tomography, ultrasound of the hip joints, ultrasound of the hip joints with color doppler mapping. [9, 11, 16]

For diagnosis of the efficiency of the antioxidant treatment we used: determination of hydroperoxides lipids, malonic dialdehyde, vitamin E, diene conjugates, ceruloplasmin in the blood plasma[5, 14], as well as the results of ultrasound with color doppler mapping. For diagnostic efficiency of complex treatment with the use of antioxidants used evaluation of the clinical picture of the disease and x-ray examination in dynamics. [16, 18]

In our work was carried out x-rays of the hip joints ultrasound of the hip joints with dopplerography, computer tomography. [12, 11]

Traditional x-ray examination in the early stages of aseptic necrosis of the femoral head of pathological changes does not reveal. X-ray examination is not always possible to answer the question about the exact location and size of the pathological process, the state of cartilage and paraarticular tissues. [11]

For the assessment of treatment outcomes, taking into account radiological and clinical data, the use of a unified classification DLCP, developed by The St. Petersburg children's orthopedic institute them Turner in 1987. [15]

To the perspective of modern methods of x-ray diagnostics include computed tomography (CT), which allows early to recognize the symptoms of aseptic necrosis of the femoral head [9]. CT allows to reveal the early stage of avascular necrosis of the femoral head. The tomograms noted the decrease in the density of bone structures in the affected limbs compared with the healthy. CT provides layer by layer, polypositions to explore the structure of the head and neck of the femur, to produce qualitative and quantitative assessment of the head of the femur and the acetabulum with the definition of public relations of the articular surfaces, the size of cystic cavities and their correlation with areas of sclerosis bones, as of the subchondral bone tissue [9].

Ultrasound with doppler ultrasonography to assess regional blood supply with different pathology of hip joints in children, is an important method for evaluating the efficiency and adequacy of treatment, load management and functional therapy. The previously angiography is not widely spread, as it is invasive method and is intended, basically, for a single study. Modern ultrasonic devices, with the possibility of color doppler flow mapping, provide the highest resolution diagnostic images of ligaments, tendons, cartilage tissue. The possible evaluation of the vascular reactions in the area of the detected changes, as well as monitoring of treatment [21]. The method is highly informative, non-invasive, fast in performance in the real-time mode, with the possibility of multiple implementation and evaluation of the dynamics of the process is relatively cheaper. Today ultrasound, undoubtedly, is the method of choice in the diagnosis of changes in various organs, including changes in the hip joints [9].

Evaluation of effectiveness of complex treatment of patients with DLCP with the use of antioxidants was held on the 3-point system M.M. Kaparov (2005) with the clinical and x-ray picture.[7]

The lack of clarity in the etiopathogenesis osteochondropathy femoral head leads to erroneous treatment tactics. A very important one view on etiology and pathogenesis DLCP, and hence the common views on the tactics of the treatment. [9]

In the last decade in the domestic and foreign literature emphasizes the need for the complex nature of the treatment DLCP.[9] This implies that underlying conservative methods of influence on the pathological process, traditionally including orthopaedic and physiotherapeutic activities, if necessary, can be combined with operational methods. [16]

Medicamental therapy is aimed at improving the supply of the hip joint tissues of oxygen, improvement of capillary blood flow, reducing blood viscosity [1]. With this purpose, some authors recommend trental, which has vasodilating, anticoagulant and weak antioxidant action [2], or curantylum [2]. Used drugs aimed at restoring the metabolism of cartilage. [10,15]

All the methods of surgical treatment directed on improvement of trophism of the femoral head. These include tunnelization neck of the femur a bunch of pins or pins with the introduction of the neck of the femur of proteolytic enzymes (chymopsin, trypsin). There is also alloplasty in the neck thigh muscle flap on the supply vessel. All the more widely in the treatment of to date used high technology, which are treated by minimal invasive and effective enough. In some clinics to revascularization of the femoral head has developed and introduced into practice a method revascularizing laser osteoperforation neck of the femur with the use of high-intensity laser radiation. Other authors offer to restore and increase the blood flow in line with the dominant arteries use of endovascular double barreled shotguns balloon catheter, entered percutaneously in the femoral artery below the bifurcation with deep artery of the thigh. Laser osteoperforation the femoral neck.[10, 15]. When inefficiency of conservative therapy to accelerate the process of reparation carry out implantation in the region osteochondropathy bioactive polymer compositions on the basis of H-vinylpyrrolidone and methyl methacrylate with medicinal fillers under arthroscopic control. [10, 15]

Identification of trends to subluxation hips and progression of structural changes in the head of the femur (broken line of Shenton, decentering, necrosis more than half of the femoral head, кистевидная restructuring in the neck, increase of age- cervico diaphyseal angle and angle antetorsii) with dynamic x-ray examination serves as the indication for the operative treatment. Surgical treatment of the disease Perthes is aimed to achieve the decompression of the joint, to improve blood supply to the femoral head and the concentration of the femoral head in the hollow. The existing or expected decentration in hip joint (in the case of total and subtotal destruction) to preserve or restore the shape and size of femoral head is required her centering in

the acetabular depression [12] in connection with than all of conservative and operative methods of treatment are divided into providing and not providing accumulate head. [2, 8]

Currently in Scientific Research Institute, Children's Orthopedic of the. G.I. Turner corrective osteotomy is supplemented in some clinical cases rotary transposition of the acetabulum in Salter. The operation is applied when expressed increasing the width of the epiphysis, increase of angle antetorsii, a subluxation of the hip. [13] In the Russian Scientific Center «Restorative Traumatology of the academician G.A. Ilizarov» method in the treatment of illness Perthes is used transosseous compressive-distraction osteosynthesis. The diagnosis is an indication for surgical treatment. Surgical task is to change the load profile at the hip joint by a subtrochanteric osteotomy, perceiving this operation as osteotomia medicata. The intersection of the bones in subtrochanteric region is a powerful stimulating factor in the restoration of the power of the femoral head in the conditions of altered anatomical situation. [4, 8]

After removing the locking devices are massage, therapeutic gymnastics, acupuncture and physical therapy in outpatient conditions or in a specialized sanatorium. The question of load on a limb (partial or complete) is determined individually for each patient depending on the degree of recovery of structure and form of the head of the femur, which define by x-rays.[14]

Proceeding from all aforesaid treatment on the initial (to X-ray) stage DLCP should be first of all pathogenic, and include symptomatic therapy. Both types of therapy have equivalent value, as without addressing the main factor and the reasons supporting the disease is not can be quick and complete recovery of the proximal epiphysis of the head of the femur, and even after the operation the disease will be a long and stubborn character.[3]

The positive side of the conservative methods of treatment is their relative simplicity and non-invasive, possibility of treatment in out-patient conditions, as well as the ability to influence on pathogenetic part of the disease.[15]

The greatest distribution was received by physical methods of treatment. In recent years, the experience of manual therapy techniques aimed at correction of the pelvic girdle and spine, manipulation techniques are carried out only in the discharge of the spine, only in lying position with the use of soft traction, do not apply shock techniques.[7, 16]

Of physical methods of treatment of the most widespread: classical massage, therapeutic gymnastics, physiotherapy, electrical stimulation of muscles, mud, hydrotherapy and kinesitherapy. [7, 12, 15]

Medicamental therapy at БИКИИ should be aimed at improving the supply of fabrics hip joint oxygen, improvement of capillary blood flow, reducing blood viscosity. [2]

On the summary data, conservative treatment brings good and satisfactory results in 24-62% of cases, surgical - in 47-83% of cases. [2, 3]

However, in all methods of treatment, in our opinion, is not enough method, which is capable to influence the pathogenetic processes and prevent changes to an irreversible stage necrotic parts, including by preventing the expansion of нейродистрофических tissue and vascular reactions of increasing the efficiency of spent treatment. In our opinion this method is an antioxidant therapy in a complex treatment of DLCP. [5,14]

The most effective in the quality of the links raising resistance of an organism to a variety of negative impacts are the compounds of pyrimidine series. [2] They are able to accelerate the regeneration of the skin, mucous membranes, muscles, bones, tendons, various divisions of the nervous system. Earlier in his work E.V.Ped in 2000 used emoxipine. Intraosseous summary of emoxipine to the site of damage decreases in the activity of lipid peroxidation, which improves the clinical and radiological indices of the pathological process, reduces the severity of the pineal gland and contributes to a more rapid recovery of bone structure and form of the femoral head.[2]

The drug of choice in our study is mexidol, which corrects violations in the regulatory and microcirculate systems, that is expressed in the fact, that causes the elimination of spas bearing microvessels, and also has a modulating effect on the activity of membrane binding enzymes, ion channels and receptor complexes, enhancing the ability for the binding of ligands, increasing the activity of neurotransmitters and activation of synaptic processes. Thus, provides multifaceted biological action: anticoagulant, angioprotective, prolonged antioxidant. That is, has an impact on almost all the parts of the pathological system, which forms the disease. [5]

Thus, in view of differences of creators in the etiopathogenesis and the low efficiency of treatment determine a large variety of conservative and operative methods of influence on the pathological process. It is difficult to disagree with the common point of view that the approach to the treatment of children with DLCP should be differentiated [19], and the treatment to be comprehensive and include conservative methods of influence on all the links of the pathogenesis of the disease [10, 12], and also include various methods of surgical correction [2, 3, 4, 8], depending on the stage of the process with antioxidant protection in the process of treatment. [5]

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Modern Models of Moral Medicine

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Summary: This article briefly compares three models of moral medicine, from which the "contract" model is recognized as meeting the requirements of most medical ethics.

Keywords: ethical medicine, models of moral medicine, paternalism, partnership, psychiatry.

Modern medical ethics is considering the vast number of new and difficult ethical issues: euthanasia, cloning, compulsory treatment of alcoholism and drug addiction, an artificial coma, artificial insemination, "pill happy", a transplant of vital organs, brain death.

The dilemma of "paternalist" ("Trustees") and "nonpaternalist" ("partner" or "peer") approaches (models) is the core to modern medical ethics.

"Paternalist" model of physician-patient relationship is based on several assumptions: a) in terms of healing human health and life are by far the priority values, and b) doctor's ethical stance is reflected in the principle of "Providing patient care, has not caused him any harm", and c) the principle deprives the patient's ability to make their own decisions and shifts it to the doctor. Thus, the physician shall have a way of "Father" (a Latin word Pater), or "parent", and the patient is properly vested with "Baby." The word "Father" has traditionally served as a metaphor for God and the priest, and, accordingly, the physician shall have the status of unquestionable authority.

"Paternalist" model has played an important role in the history of medicine. With the approval of paternalist physician-patient relationship due to bridge the gap of morality and life, the establishment of ethics in medicine. But at the same time, the moral authority of the physician has such an impact on the patient that suppresses the freedom and dignity.

Harbinger of the crisis in the Russian medical paternalism was a crisis of involuntary treatment in psychiatry in the late 80s, early 90s. Twentieth century. Rod "problematic situation" in the provision of psychiatric care was involuntary treatment as a consequence of "paternalist" model of medical ethics. Up until the late 88-ies of XX century, compulsory hospitalization of the mentally ill was considered an overwhelming immutable social norm.