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Differentiated Approach to the Treatment of Juvenile Dysmenorrhea in Adolescent Girls

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Resume. Adolescence is a transitional period in a person's life, which is characterized by both physiological and emotional-personal changes.

One of the major physiological changes that occur in adolescent girls is menarche, which is often associated with the problem of irregular menstruation, abnormal pubertal uterine bleeding, and primary dysmenorrhea (PD).

PD is one of the important tasks of pediatric gynecology, which is associated with its high frequency of occurrence and with its socio-psychological aspect, which worsens the quality of life of adolescent girls.

According to recent data, this pathology may be a predictor of other diseases and pathological processes that manifest as PD in adolescence. One such example is adenomyosis, which may have its onset in adolescence, but the diagnosis, according to the EIBKE, can take many years, from about 7 to 10 years.

Keywords: physiological changes, adolescent girls, menarche, adenomyosis, pathological processes.

Relevance. According to the literature data of domestic and foreign colleagues, the prevalence of PD among adolescent girls varies from 8% to 90%. And the severe course of PD, which leads to a decrease in social activity, loss of working capacity, is 15% of cases, which is why this pathology is a serious medical and social problem that needs to be dealt with.

Among the causes of school absenteeism, PD ranks first and among the urgent reasons for hospitalization of adolescent girls in a hospital - the fourth place (13%).

There are a number of theories of the occurrence of PD, but none of these hypotheses fully explains the etiology and pathogenesis of this pathology, especially the development of its severe forms, and the available methods of treatment are not effective enough.

It is important to note that the main theory of the occurrence of PD is considered to be prostaglandin, and today the first-line treatment drugs are non-steroidal anti-inflammatory drugs (NSAIDs), the appointment of which is pathogenetically justified at any age and has a high level of evidence [18, 61, 66, 79, 103 , 115]. But having a wide arsenal of these drugs, the therapy does not always lead to a decrease in the frequency of PD, but only has a symptomatic effect in the form of a temporary relief of pain, and in severe PD, in most cases, there is no analgesic effect at all.

But often pain is not the only manifestation of this disease. Sometimes, in the absence of painful sensations, neurovegetative, psycho-emotional and metabolic-endocrine symptoms prevail, reflecting the low adaptive ability of the whole organism, which is often due to the presence of a premorbid background.

Such a condition can be connective tissue dysplasia (CTD), which is characterized by the manifestation of clinical symptoms in adolescence, up to the development of severe multi-organ and multi-system forms. CTD remains an understudied problem, and recently, in the severe course of PD, a special place has been given to this particular pathology.

Numerous studies have shown that endothelial dysfunction occurs in CTD, which is also described in PD, leading to various disorders in all organs and systems. Unlike hereditary connective tissue disorders (HCTD) or differentiated forms with a certain type of inheritance and a clear clinical picture, CTD, i.e. unclassified form, does not have a specific clinical symptom complex and is widespread in the population. This pathology may not manifest itself for a long time and proceed in a mild form, but any provoking agent can cause manifestation and even lead to death. These factors can be stress, physical activity, pregnancy, childbirth, infections, injuries, surgical interventions, etc.

Purpose of the study. Improving the efficiency of early diagnosis and developing a differentiated approach to the treatment of adolescent girls suffering from primary dysmenorrhea, taking into account etiopathogenetic factors.

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Material and research methods. 100 patients with PD were examined and treated. The choice of the direction and methods of research, setting goals, objectives, planning and conducting various studies, performing calculations, statistical processing of the obtained clinical and instrumental data and summarizing the results, writing and designing the dissertation and abstract were performed by the author independently.

Primary dysmenorrhea is painful menstruation in the absence of pathology from the pelvic organs.

Results of the study and their discussion. A study of 600 women, of whom 72% reported dysmenorrhea. 15% of them had severe dysmenorrhea. 50% of these girls and women were absent from school or work at least once a month due to this pathology. But it should be noted that the statistics do not fully reflect the true prevalence of PD, because. in mild cases, most adolescent girls do not seek medical attention and/or self-medicate.

This fact suggests that little attention is paid to the problem of PD, although this pathology is not only a medical problem, but also a socio-economic one, since patients suffering from this pathology become disabled every month. With a rough estimate, these patients due to PD become disabled for 5.5 years of their lives. Recurring periodic pain and its expectation affects the formation of personality and contributes to the development of neurotic conditions, up to the development of severe mental disorders.

The hereditary factor is important, because. Approximately 30% of adolescent girls have maternal relatives suffering from PD.

According to Kagata et al., late and short sleep less than <6 hours leads to more severe PD. This is due to the effect of melatonin on COX activity. But it must be remembered that PD can be a factor in sleep disturbance.

Some authors believe that adverse environmental effects (hypothermia, infectious diseases, etc.) and stressful situations (mental trauma, mental and physical overload, etc.) can lead to PD.

Thus, the problem of PD is associated with a high frequency of its occurrence and with its socio-psychological aspect.

The basis of any pathology is cell damage. Under the influence of damaging factors, cell membrane structures are damaged, in which phospholipids, receptors, protein ion carriers and ion pumps can undergo destruction. Due to the destruction of phospholipids, cell membranes are destabilized, the electrolyte balance is disrupted, leading to disruption of the ion pumps and an increase in the concentration of intracellular

To develop a pathogenetically based diagnostic and treatment algorithm for the management of patients suffering from PD, it is necessary to understand the causal relationships of this disease and concomitant disorders that lead to cell damage and cause pain.

To date, it has been established that after the regression of the corpus luteum, there is a sharp drop in the level of estrogen and progesterone, which causes menstruation. It should be noted that a decrease in progesterone levels is a trigger for the metabolism of arachidonic acid, which leads to the activation of leukocytes. The latter causes an increase in the activity of pro-inflammatory cytokines, which are a group of interleukins (IL) -1, -6, -8, tumor necrosis factor a (TNFa). It is important to note here that studies have been conducted that have shown that in the luteal phase of the menstrual cycle, the endometrial stroma is represented mainly by leukocytes (about 40%), macrophages, mast cells, eosinophils, monocytes and other cells of the immune system. In turn, pro-inflammatory cytokines cause a change in the activation of matrix metalloproteinases (MMPs), leading to the destruction of the extracellular matrix of the basement membrane of the endometrium, and the latter, in turn, activate the cyclooxygenase and lipoxygenase pathways of arachidonic acid metabolism, thereby causing rejection of the endometrium - menstruation itself. These processes occurring in the endometrium are similar to hypoxia and inflammation.

Currently, the prostaglandin theory provides the main explanation for the occurrence of dysmenorrhea. According to this theory, due to a violation of the metabolic cascade of arachidonic acid, hypersecretion of prostaglandins (Pg) occurs in the endometrium. After cell damage by various altering agents, Ca-dependent enzymes are activated, including phospholipase A2, under the influence of which arachidonic acid is released from phospholipids, which form the basis of the cytoplasmic membrane. Damaging agents can be pro-inflammatory cytokines Il-1, -6, -8, TNFa, bradykinin, histamine, etc. The latter arise due to a violation of neuromuscular excitability, in which there is a violation of intracellular Ca2+ homeostasis in the cell and vasospasm. All of the above processes cause an increase in intrauterine pressure, vasospasm, impaired blood supply to the myometrium and its hypoxia. As a result of the latter, the permeability of the cell increases and pain mediators such as Pg, H+, K+ and others leave the cell into the extracellular space. There they act on the pain receptors of the uterine afferent fibers, activating them, and pain occurs.

However, in addition to the cyclooxygenase pathway for the conversion of arachidonic acid, there is also a lipoxygenase pathway, which may be one of the pathological links in the development of PD. Under the influence of phospholipase A2, along with COX, another enzyme, 5-lipoxygenase (5-LPO), is simultaneously activated, which leads to the synthesis of leukotrienes from arachidonic acid. At the beginning, leukotriene A4 (LTA4) is synthesized, which goes through several stages of transformation. As a result, different types of leukotrienes are formed - leukotriene B4

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(LTB4), C4 (LTC4), D4 (LTD4) and E4 (LTE4), which are found in different tissues of the body. The last three types of leukotrienes (LTC4, LTD4, and LTE4) are involved in the body's immune responses and can lead to edema, smooth muscle spasm, eosinophilia, and anaphylaxis.

According to studies in patients suffering from PD and endometriosis, leukotrienes are formed in the mucous and muscular layers of the uterus.

Benedetto and Nigam noted that, on average, 30% of adolescent girls with PD were resistant to COX inhibitors, and Rees in their study noted that in girls with primary dysmenorrhea who did not respond to COX inhibitor therapy, Pg concentrations in menstrual blood did not different from the values in the control group.

In 2010, a double-blind, placebo RCT was conducted by a group of researchers who studied the efficacy of montelukast treatment of PD in patients who were not susceptible to prostaglandin synthetase inhibitors. The researchers observed a more than 2-fold decrease in the intensity of menstrual pain compared to the placebo group.

Thus, leukotrienes can be one of the factors in the occurrence of PD and endometriosis, and their selective inhibitors can be considered as a method of therapy for patients who do not respond to treatment with COX inhibitors.
To date, one of the popular theories of the occurrence of PD is also hormonal, according to which painful menstruation occurs due to absolute or relative hyperestrogenemia. Estrogens can activate the contractile activity of smooth muscles by increasing the activity of COX, while progesterone, on the contrary, can slow down by reducing the activity of phospholipase A2. On the other hand, it should be noted that PD also occurs in hypoestrogenemia and hyperprogesteronemia. In addition, this pathology is often found in adolescent girls with normal levels of sex hormones.

Research over the past 20-30 years has shown that chronic pain conditions such as endometriosis, headache, irritable bowel syndrome, fibromyalgia, interstitial cystitis, arthrosis, and various neuropathic pains are associated with significant, widespread, and sometimes long-term chemical and functional changes in the central nervous system, even at rest.

Conclusion. Similar studies have also been carried out with respect to PD. positron emission tomography (PET) study of cerebral metabolism in women with PD and revealed its violations when compared with the control group. A group of authors performed voxel brain morphometry to compare increases and decreases in total and regional gray matter in 32 PD patients compared with healthy adolescents, and found an abnormal decrease in gray matter volume in areas involved in pain transmission in PD patients. Then the authors came to the conclusion that changes occurring in the central nervous system can be observed not only in diseases accompanied by chronic pain, but also in such cyclic pain conditions as PD.

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