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PECULIARITIES OF THE DEVELOPMENT OF CHRONIC PELVIC PAIN RELATED COMPONENTS IN PERITONEAL ENDOMETRIOSIS

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ОСОБЕННОСТИ ФОРМИРОВАНИЯ КОМПОНЕНТОВ ХРОНИЧЕСКОЙ ТАЗОВОЙ БОЛИ ПРИ ПЕРИТОНЕАЛЬНОМ ЭНДОМЕТРИОЗЕ

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The article includes the results of the complex study of cytokine and serotonin status as pathogenic chronic pelvic pain related factors in peritoneal endometriosis. The distinctive features of the development of the syndrome associated with the severity and character of the pelvic pain due to peritoneal endometriosis have been revealed.

Key words: chronic pelvic pain, peritoneal endometriosis, cytokines, serotonin

Представлены результаты комплексного исследования цитокинового и серотонинового статусов как факторов, участвующих в формировании патогенетических компонентов хронической тазовой боли при перитонеальном эндометриозе. Выявлены особенности формирования данного синдрома в зависимости от интенсивности и характера течения тазовой боли при перитонеальном эндометриозе.

Ключевые слова: хроническая тазовая боль, перитонеальный эндометриоз, цитокины, серотонин

Endometriosis is one of the most common gynecologic disorders and is found in approximately 70 % of patients with chronic pelvic pain [1]. Approximately 25 % of women with pelvic pain were diagnosed peritoneal endometriosis by laparoscopy. Numerous investigations of different aspects of chronic pain due to peritoneal endometriosis were performed but none of the developed methods resulted in complete regression of chronic pelvic pain or allowed avoiding recurrence of the disease [3, 4]. This can be referred to a complex structure of the chronic pain which is heterogeneous in nature as a rule and is presented as a combination of symptomatic complex, demonstrating the presence of nociceptive, nuerogenic and psychogenic constituents [2, 5]. Though different chronic pain related factors in peritoneal endometriosis have been studied. Complex studies of its pathogenic components, especially in different bodily pain and character of pain syndrome are not still available. At the same time registration of these pathogenic peculiarities allows developing more effective medical suppression for different stages of chronic pelvic pain due to peritoneal endometriosis.

The aim of the study was to assess the peculiarities of the cytokine and serotonin status as factors providing formation of the components of chronic pelvic pain caused by peritoneal endometriosis of different intensity and character of the painful syndrome.

Material and Methods. We studied 195 female patients with chronic pelvic pain due to peritoneal endometriosis and 30 practically healthy women (control group) between 25–42 years of age. The groups were comparable regarding the main indexes. Laparoscopy performed for pelvic pain syndrome revealed stage II and III peritoneal endometriosis in all the patients. The data were confirmed by histological examination. 109 (55.9 %) patients were diagnosed primary peritoneal endometriosis, 86 (44.1 %) had the recurrent pelvic pains due to peritoneal endometriosis. The severity of pain was determined by visual analog scale (VAS).

According to the severity of diagnosed pain syndrome and according to the character of the disease (primary or recurrent) the patients were divided into four clinical groups. The patients of the group 1 (n=53, VAS 4–6 grades) and the group 2 (n=56, VAS 7–10 grades) were revealed primary peritoneal endometriosis. The patients of the group 3 (n=45, VAS 4–6 grades) and the group 4 (n=41, VAS 7–10 grades) demonstrated recurrent chronic pelvic pain. The fifth group was a control one (n=30). All patients underwent complex clinical studies of their cytokine profile, serotonin antinociceptive neurotransmitter in the peripheral blood as well as their psychic and emotional status using Spilburg – Hanin tests and questionnaire SF-36.

The statistical processing was carried out using the descriptive statistics. The difference of central parameters was made using the criterion of Mann – Whitney or there was applied the criterion χ^2 to compare the frequencies. There was used the add-in in the program EXCEL «Analysis package» and the statistical program package STATISTICA V.8 as well as. The differences at $p<0.05$ were authentic.

Results and Discussion. Among the patients with the primary peritoneal endometriosis the cases with chronic pelvic pain of 1–2 year duration were the most common and accounted for 63.3 %. The high incidence of recurrent peritoneal endometriosis was revealed among the patients with 3–5 year (52.3 %) and 6–8 year (47.7 %) duration of this syndrome. Besides chronic pelvic pain 57 (29.2 %) patients were revealed dysmenorrhea and 30 (15.4 %) demonstrated dyspareunia. All patients had such emotional disturbances as sleeplessness, fatigue, changeable mood, irritability, emotional instability, anxiety, phobias, and others. Our studies didn't reveal any association of marked chronic pelvic pain with the stage of the peritoneal endometriosis, its location, the type of heterotopias, as well as the character of the disease (primary or recurrent).

Summing up the data on the changes of cytokine force in peripheral blood it is possible to suggest the presence of inflammatory component in the pathogenesis of chronic pelvic pain of different severity and character (Fig. 1). At the same time the patients with primary disease demonstrated statistically significant increase ($p<0.05$) of anti-inflammatory interleukin concentration when the pain got worse (group 1 and 2). It was compensated to a great extend by the turn of anti-inflammatory force with delayed increase. It shows the anti-inflammatory index that represents the correlation in the interleukin-1β family. In case of mild recurrent chronic pelvic pain maximum permissible domination of inflammatory cytokine level ($p<0.05$) and some inhibition of anti-inflammatory level was revealed in the peripheral blood of patients with peritoneal endometriosis of various stages. These data have been confirmed by anti-inflammatory index. The fourth group of patients with recurrent severe pelvic pain demonstrated statistically significant depression of pro- and anti-inflammatory cytokine force ($p<0.05$) with the decrease in absolute index of interleukin level that indicates «the false stabilization» determined by anti-inflammatory index and is the evidence of failure in adaptive capacity as well.

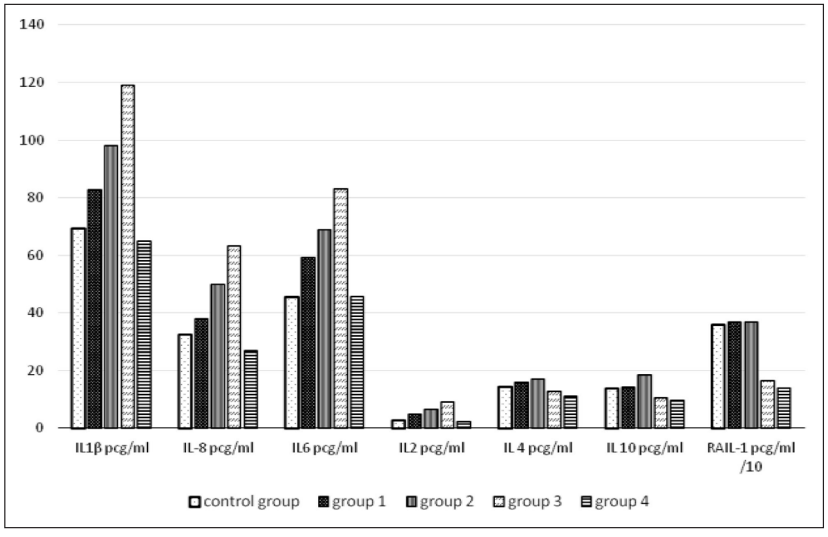

Fig. 1. Cytokine status in patients with various chronic pelvic pains due to peritoneal endometriosis

In all groups of patients the level of serotonin in peripheral blood was reduced as compared with the control group ($p<0.05$). In spite of the fact that the patients considered their pain as mild it should be mentioned that the serotonin level in patients of the third clinical group with median 150.1±1.8 ng/ml as well as in the patients of the first group with median 164.0±1.2 ng/

ml ($p<0.05$). was reliably different. The mean level of serotonin in the peripheral blood of patients in the second and fourth groups was 110.41±1.4 ng/ml, Me – 109 and 96.1±1.7 ng/ml, Me – 95, respectively. The level of serotonin in groups 2 and 4 was significantly low as compared with the clinical groups 1 and 3 ($p<0.05$). At the same time the quantity of serotonin in patients of the group 4 was reliably lower ($p<0.05$) than in group 2. However according to VAS the pain in these groups was objectively identical (7.7±0.1 and 7.7±0.1 respectively).

Our studies have demonstrated the impairment of serotonin status as the index of pain intensity in all the patients with chronic pelvic pain. The reduction of serotonin level worsened in pain reinforcement. In recurrent identical pains serotonin synthesis is significantly depressed. This is associated with cytokine misbalance and can be the evidence of analgetic system depletion and development of psychogenic component of pain syndrome in recurrent chronic pelvic pain due to peritoneal endometriosis.

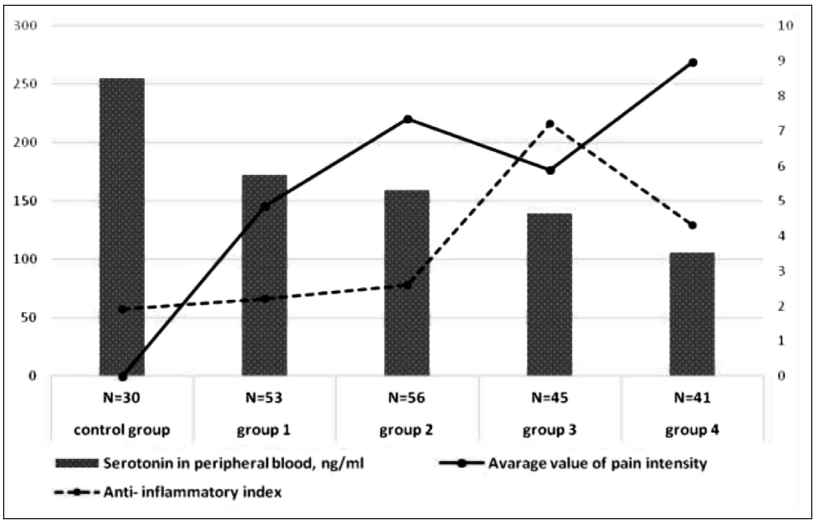

Fig. 2. Correlation of serotonin level index in peripheral blood with severity of pelvic pains and proinflammatory index in various chronic pelvic pains due to peritoneal endometriosis

The dynamic of the psychic and emotional status impairment was identical. The levels of reactionary and personal anxiety, as well as the quality of life assessment depend on the pain syndrome severity; but these indices were noted to be significantly low in group 3 and 4 with recurrent chronic pelvic pain ($p<0.05$) that is in chronic persistent pain syndrome. It should be mentioned that psychosomatic disorders are closely associated with cytokine and serotonin status (Fig. 2).

Conclusions. Our studies have demonstrated that in pain syndrome caused by peritoneal endometriosis intractable immune inflammation initiating chronic inflammatory process leads to persistent painful symptoms and promotes prolonged hyperexcitability of nociceptive system that causes serotonin level reduction. At the same time in the patients with recurrent chronic pelvic pain due to peritoneal endometriosis the disease was found to have a reliably long course with aggravated nociceptible, neurogenic and psychogenic pain related components. «Relation» of chronic pain and psychoemotional disorders can be referred to general pathogenic mechanisms as well as to the failure of the neurotransmitter exchange in the central nervous system. It is serotonin that controls such function of the transmitter system of the brain as: opiate, dopaminergic, and adrenoceptive. Insufficiency of serotonin energetic system of the brain is evident both in chronic pelvic pain and in psychosomatic disorders. Thus the study of the chronic pelvic pain related factors in primary peritoneal endometriosis is characterized by such distinctive features as intensification of nociceptible and neuropathic pain related components depending on the bodily pain. However, only marked duration of the pain syndrome (recurrence) results in development of dominant psychogenic pain related component that is medically resistent.

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