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Early Diagnosis of Precancerous Diseases of the Uterus

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Resume. Currently, organ-preserving operations in patients with uterine myoma occupy a significant place in operative gynecology. However, any surgical methods of treatment do not eliminate the etiological and pathogenetic causes of the disease, so there is always a significant proportion of the likelihood of its recurrence. One of the important indicators of the effectiveness of the treatment of fibroids is the frequency of recurrence of the disease.

Keywords: cervical cancer, malignant tumors, female genital organs, screening, female population.

Relevance. In this regard, to assess the effectiveness of the treatment, as well as to prevent relapses, the most appropriate approach is to select criteria that allow for early diagnosis, for which a number of laboratory diagnostic methods are used. The earliest predictors of disease recurrence, in our opinion, are indicators that characterize the intensity of the metabolism of connective tissue biopolymers, tk. tumor growth and development (including fibroids) is largely associated with local destruction of these components, which is accompanied by their release into the systemic circulation.

Purpose of the study. The purpose of this study is to evaluate the effectiveness of conservative myomectomy and uterine artery embolization in patients with uterine myoma using biochemical markers of connective tissue biopolymer metabolism.

Material and research methods. A biochemical study of blood serum and daily urine was carried out in 71 patients with uterine myoma. 50 women underwent conservative myomectomy, including laparotomy removal of the focus of fibroids (Group 1). The age of women in this group ranged from 23 to 50 years. The mean age of the patients was 37.2 ± 3.5 years. The duration of the disease with uterine myoma was 5.1 ± 0.6 years. Indications for conservative myomectomy were hypermenstrual and pain syndromes in combination with chronic gynecological diseases. As a result of the operation, reproductive function was preserved for all women.

The second group included 21 women who underwent uterine artery embolization. The inclusion criteria for patients in this group were: the size of myomatous nodes from 2 to 10 cm, the absence of severe extragenital pathology, the absence of pregnancies and hormonal treatment within 4 months before treatment. Women with subserous myoma nodes on a thin base were not included; combined gynecological pathology requiring surgical intervention and severe allergic reactions to iodine preparations, coagulopathy. The age of patients of the 2nd group ranged from 23 to 45 years. The average age in the group was 33.5 ± 2.4 years, the duration of the disease was 3.9 ± 0.4 years.

All patients underwent blood sampling from the cubital and uterine veins before surgery. Daily urine was collected the day before the operation. A re-examination was performed 6 months after the operation.

In the blood serum of patients, the concentration of degradation products of the organic matrix of the connective tissue was determined: power (SA), glucuronic (HA) acids and hexosamines (HA), as well as the content of sex hormones - estradiol and testosterone. In daily urine, the content of hydroxyproline, sialic, uronic acids and hexosamines was determined.

The concentration of sialic acids in biological fluids was determined using reagent kits from Sialotest 100 (St. Petersburg). The concentration of uronic acids was determined by the thiobarbituric method, hexosamines - with Ehrlich's reagent after hydrolysis in hydrochloric acid. The content of hydroxyproline in the urine was found by the Ehrlich reaction, after hydrochloric acid hydrolysis in sealed ampoules. The content of estradiol and testosterone was determined by radioimmunoassay using an analysis kit from Immunotech (France), activity was calculated and concentration was determined on a Tracor Europe gamma counter (Holland).

As a comparison group, we studied similar biochemical parameters of 30 practically healthy women (without gynecological pathology) aged 30 to 50 years.

The results of the laboratory study were presented as the arithmetic mean (M) and standard deviation (SD). The significance of differences with the control group was assessed using the nonparametric Wilcoxon W test for



unrelated samples. Intergroup differences were assessed using the nonparametric Kruskal–Wallis multiple comparison test.

Results of the study and their discussion. We found that the concentration of most of the studied biochemical markers in the cubital vein in the examined patients of both groups before the start of treatment statistically significantly exceeded the corresponding age norm. Only the level of SC in patients of the 1st group did not differ significantly from the norm. In the uterine vein, increased HAA and GA values were also observed in patients of both groups, while the level of SC in the local blood flow in both groups did not differ significantly from the norm, while its average values were even slightly lower than the average of the control group.

Six months after surgical treatment, the concentration of SC in the systemic circulation in patients of the 1st group practically did not change, remaining within the normal range. In patients of the 2nd group, the level of this metabolite tended to decrease, while its initial elevated numerical values returned to the normal range. After treatment, in patients of both groups, there was also a significant decrease in the level of HUA in the blood serum relative to the start of treatment: in the first group by 38% ($p = 0.02$), in the second - by 34% ($p = 0.03$). However, the level of HUC after treatment in both groups remained significantly elevated relative to the norm. There was no significant change in the concentration of GA in patients of both groups 6 months after the operation relative to the period before the start of treatment, the values of this metabolite remained at a high level relative to the age norm.

Thus, the initial level of HAA, GA and hydroxyproline excretion in patients of the 2nd group was significantly higher than the norm, while in women of the 1st group only the values of oxyproline excretion were elevated. However, six months after the treatment, the concentration of SC, HUA in the daily urine of patients in both groups significantly increased both in comparison with the initial values recorded before the start of surgical treatment, and in relation to the corresponding age norm. The level of HA in the urine of women in both groups after treatment was significantly higher than normal. At the same time, if in the 1st group the increase in the concentration of GA relative to the start of treatment had significant differences, then there were no significant changes in this metabolite after treatment in patients of the 2nd group relative to the initial level. Excretion of hydroxyproline in patients of both groups 6 months after surgery significantly decreased relative to the initial (preoperative) values by almost one value: by 35% ($p = 0.05$) in the first group and by 33% in the second ($p = 0.05$).), however, the mean concentrations of hydroxyproline in the urine after treatment were still significantly higher than normal.

The study of the concentration of estradiol in the luteal phase of the menstrual cycle showed that in the examined women of both groups, the concentration of this hormone in the systemic circulation was slightly below the norm, but in the uterine vein in patients of the 1st group, such a decrease was significant (figure). In the follicular phase of the cycle, the average values of the level of estradiol in the systemic and local circulation in women of both groups were significantly increased relative to the norm. In the uterine vein in patients of both groups, we also noted a significant variation in the concentration of estradiol in the follicular phase of the menstrual cycle, both in the direction of low and high concentrations, however, we did not reveal significant differences between the local and systemic concentrations of estradiol.

Six months after the end of treatment, the concentration of estradiol, measured in the luteal phase of the cycle, in patients of both groups statistically significantly, almost two times, decreased both relative to the initial preoperative values and relative to normal values. In addition, we found that the concentration of testosterone in women of both groups before the start of surgical treatment was almost twice as high as the norm. After treatment, the level of this hormone in the blood serum of patients in both groups remained significantly elevated.

Conclusion. The results of the study revealed one general trend: in patients with uterine myoma after treatment, regardless of the type of surgical intervention, there was an increase in the intensity of excretion of degradation products of connective tissue biopolymers from the body. There was a decrease in the concentration of decay metabolites in the blood serum against the background of an increase in their excretion in the urine. This observation is undoubtedly a favorable factor indicating the normalization of metabolic processes in the uterus and the effectiveness of the methods used to treat fibroids. This is supported by the fact that in all patients six months after treatment, not a single relapse was observed. It is also undoubted that the effectiveness of the methods used is largely related to the choice of indications for the use of a particular technique.

The concentration of estradiol (pg / ml) in the systemic and local blood flow in the examined women in different phases of the menstrual cycle. Note. LF, luteal phase; FF, follicular phase; PV - ulnar vein, MV - uterine vein, LV normal - ulnar vein normal (healthy women)

Nevertheless, despite the positive dynamics of the recovery of biochemical markers, one important circumstance should be noted. We noted that many of the studied blood serum parameters after six months of treatment, despite the postoperative decrease, remained at a high level relative to the norm. Such an observation, most likely, indicates the incompleteness of the recovery and regenerative processes in the operated organ by the sixth month



after the operation. An important practical conclusion from this is that after six months of treatment, the likelihood of relapse remains, so the timing of the follow-up examination should be carried out at a later period - a year and a half after the operation.

It is also interesting that after surgical treatment, the examined patients showed a pronounced decrease in estradiol in the blood, which, apparently, indicated a decrease in the hormonal activity of the ovaries in women after surgery. At the same time, an almost twofold decrease in the concentration of this hormone in the blood clearly indicates the absence of a compensation reaction, which suggests the need for hormone replacement therapy in patients in the recovery period after surgical treatment of uterine fibroids.

Thus, the use of methods of conservative myomectomy and uterine artery embolization in the treatment of uterine fibroids leads to the normalization of metabolic processes in the operated organ, associated with a decrease in the intensity of degradation of connective tissue organic matrix biopolymers.

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