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THE PECULIARITIES OF THE DATA OF INSTRUMENTAL EXAMINATIONS OF WOMEN AFFECTED BY UTERINE FIBROIDS WITH CONCOMITANT HEPATOBILIARY DISEASES

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ABSTRACT

Nowadays, women's reproductive health is a topical issue of obstetrics and gynecology, therefore, great importance is attributed to timely diagnosis and prevention of diseases that influence fertility. The topicality of the issue of uterine hyperplasia, in particular, uterine fibroids, is accounted for by the social significance of the disease. Its incidence rate is constantly growing and makes up from 30 to 50% in women older than 35 years and, according to the data of autopsy, - up to 80%. No doubt, the peculiarities of development and progression of hyperplasia are determined by the reserve potential of various systems and organs, including the hepatobiliary system. The aim of research is to analyze the results of instrumental examinations of the functional capacity of hepatocytes in women affected by uterine fibroids and functional disorders of the hepatobiliary system.

Research materials and methods. To accomplish the set objective, we used the following contemporary instrumental examination methods: ultrasonography and rheovasohepatography as well as a clinical and paraclinical analysis of caserecords of 150 women aged between 35 and 45 and affected by uterine fibroids, who were treated at the gynecological department of the Regional Perinatal Centre.

Research results. As the research result show, uterine fibroids and the related hormonal disorders often go together with functional and morphological lesion of hepatocytes. Patients affected by uterine fibroids have preconditions for the development of functional disorders of hepatocytes as they present significant disorders of hepatic hemodynamics, decreased blood supply of the liver, as a result of pre- and postcapillary resistance.

Conclusions. There is a close connection between uterine fibroids with concomitant hepatobiliary disorders and the severity of hormonal disorders, and the significant lesion of hepatocytes may be irreversible. This requires pathogenetic correction by introducing drugs with hepatoprotective and antioxidant effects.

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1. Introduction. The topicality of the issue of uterine hyperplasia, in particular, uterine fibroids, is accounted for by the social significance of the disease. Its incidence rate is constantly growing and makes up from 30 to 50% in women older than 35 years and, according to the data of autopsy, - up to 80% [1,2]. Not only does this pathology cause a decrease in working capacity and the deterioration of women's quality of life, it often leads to infertility, misbirth and preterm labor [3].

No doubt, the peculiarities of development and progression of hyperplasia are determined by the reserve potential of various systems and organs, including the hepatobiliary system. The liver plays

a major role in the maintenance of homeostasis, first of all, owing to an important stage in estrogen metabolism – “the first passage through the liver” – as well as in the realization of the positive effect of hormone replacement therapy [4].

Therefore, the problems that arise in case of hepatobiliary pathology in women affected by uterine fibroids, including the assessment of the role of hepatocytes and their functional lesion from the point of view of reproductive health and the risk of menopausal metabolic syndrome, need to be solved. The data concerning the improvement of the ways of correction and prevention of systemic disorders in women affected by hepatobiliary pathology remain quite controversial [5].

The **aim** of research is to analyze the results of instrumental examinations of the functional capacity of hepatocytes in women affected by uterine fibroids and functional disorders of the hepatobiliary system.

2. Research materials and methods. We have carried out a clinical and paraclinical analysis of case records from the gynecological department of Ivano-Frankivsk Regional Perinatal Centre for the period from 2015 to 2020 and selected 150 women aged between 35 and 45 and divided them into the following groups: Group 1 (basic group) – 60 women affected by uterine fibroids and with a positive hepatological anamnesis; Group 2 (comparison group) – 60 women affected by uterine fibroids but presenting no functional hepatic disorders; Group 3 (reference group) – 30 women of reproductive age with an unaffected menstrual cycle and no signs of hyperplasia of the reproductive system organs.

The research was carried out in compliance with the bioethical principles and the legislatively established standards and requirements regarding clinical/biomedical research, including the provisions of the Declaration of Helsinki (1964-2013), the Constitution of Ukraine and the Civil Code of Ukraine (2006), the Basics of Healthcare Legislation of Ukraine (1992), Guidelines for Clinical Research from the Ministry of Health of Ukraine No. 42-7.0:2005 “Medicines. Appropriate Clinical Practice” (2005), the Typical Regulation on Ethics Commissions in Medical Institutions Conducting Clinical Tests (Order No. 690 of 23.09.2009 by the Ministry of Health of Ukraine).

To assess the hepatobiliary function, we used the results of additional examination methods, including instrumental examinations (ultrasonography and rheovasohepatography). Rheohepatography was executed with the use of a RG-4-01 rheograph, with simultaneous recording of an electrocardiogram on an empty stomach, after 10 to 15 minutes of decubitus and while holding breath in shallow inspiration. The active electrode was placed on the skin along the mid-clavicular line on the right costal arch, the passive one – 1.0-1.5 cm below the boundary of the right lung, in the middle between the paravertebral line and the posterior axillary line. The ultrasonography of the small pelvis organs, with the calculation of the ovarian-uterine index, and the ultrasonography of the liver, kidneys, the thyroid gland and the mammary glands were executed with the use of linear and sectoral sensors for the Aloka-630 apparatus (Japan).

The methods of descriptive statistics of quantitative variables included the measures of central tendency – the assessment of the mean and the standard deviation ($M \pm m$). Categorical variables are represented as the absolute number of cases in a group and the percentage – n (%). In our statistical analysis, we calculated the significance level (p), considering 0.05 as the critical level.

3. Research results. According to the results of our complex clinical, laboratory and instrumental examinations, a certain type of chronic hepatobiliary pathology was found in 68 patients (56.67%). Chronic hepatitis of cholestatic etiology was diagnosed in 31 cases (25.8%) and chronic cholecystopancreatitis in 5 women (4.2%) affected by uterine fibroids. The prevailing type of dyskinesia was hypotonic, found in 32 patients (43.8%). Hypertonic dyskinesia was found in 9 patients (7.5%) and mixed dyskinesia – in 25 women (34.2). Hypotonic biliary dyskinesia and mixed dyskinesia were found more often in women from the basic group whereas hypertonic dyskinesia prevailed in the comparison group. Primary dyskinesia made up 24.5 % of all types of dyskinesia (18 cases).

It should be noted that in the basic group, 58 patients (96.67 ± 2.32)% were diagnosed with biliary dyskinesia, 39 women (65.00 ± 6.16)% - with acalculous cholecystitis, 17 women (28.33 ± 5.82)% - with calculous cholecystitis, 23 women (38.33 ± 6.28)% – with chronic hepatitis, 5 women (8.33 ± 3.57)% – with chronic cholecystopancreatitis and 23 women (38.33 ± 6.28)% – with nonalcoholic fatty liver disease, which indicates a statistically significant increase in the incidence of biliary dyskinesia, inflammatory processes in the gallbladder and lesion of liver parenchyma in the said category of women. In contrast, only 5 women from the comparison group (8.33 ± 3.57)% were diagnosed with hepatobiliary pathology (all of them suffered from biliary dyskinesia and one of them

(1.67 ± 1.65)% also had chronic acalculous cholecystitis), and these nosological data were obtained only after thorough examinations in the course of implementation of this diagnostic program.

The aggregate of clinical and anamnestic data and the results of objective, laboratory and instrumental examinations of women from the reference group reveal only 3 cases (10.00 ± 5.48)% of biliary dyskinesia and 2 cases (6.67 ± 4.55)% of manifestations of diffuse lesion of liver parenchyma according to the ultrasonographic data.

According to the results of liver ultrasonography, hepatomegaly of the right lobe was found in 44 patients (36.7%), 26 of which (21.7%) belonged to the basic group. The sizes of the left lobe were normal and did not differ from the data of the reference group. The examination of liver parenchyma revealed diffuse changes and unchanged liver outline and vascular pattern in 4 (6.6%) women from the comparison group and 22 (36.7%) women from the basic group. The obtained data of the ultrasound attenuation coefficient exceeded the reference values and made up (64.22 ± 1.00)% and (54.16 ± 0.06)%. The diameters of the common hepatic artery, the proper hepatic artery, the portal vein and the common bile duct were normal.

Women from the examined groups presented ultrasonographic signs of cholesterosis of gallbladder distinguished by significantly thickened gallbladder walls, reduced contractility and increased volume (up to (19.9 ± 2.9) cm³ in the basic group and up to (16.8 ± 3.1) cm³ in the comparison group). The gallbladder contractility was reduced to (32.6 ± 5.2)% in the basic group vs. (38.8 ± 6.4)% in the reference group. This can be accounted for by structural changes in the hepatobiliary organs as a result of disorders of lipid metabolism due to hormonal disorders. The gallbladder homogeneity coefficient was decreased in both groups but more significantly in the basic group (2.12 ± 0.23) in comparison with the reference group. The decreased homogeneity of the gallbladder walls is caused by the inclusion of esters of cholesterol into its structure. These processes are most characteristic of cholesterosis of gallbladder and the disorder of the motor and evacuative function is an additional proof of that. Pathological changes in the gallbladder of women affected by uterine fibroids go together with fatty liver infiltration. The established structural disorders of hepatobiliary organs suggest that they should be regarded as manifestations of dysmetabolic processes and dystrophic changes of the liver. 26.7% of women from the basic group presented ultrasonographic signs of fatty hepatosis. In this case, one can assert that hepatosis is not a disease but a syndrome reflecting significant metabolic disorders of the liver.

In view of the above mentioned considerations, we studied the condition of the regional blood flow in the livers of 60 women affected by uterine fibroids and 30 healthy women from the reference group, using rheohepatography.

The analysis of rheohepatograms of women affected by uterine fibroids shows that the initial data of blood filling of hepatic vessels (PI) were extremely decreased both in the comparison group and the basic group (0.69 ± 0.03 and 0.46 ± 0.05 respectively) in comparison with the reference group (0.78 ± 0.06) ($p < 0.05$).

We also noted an increase in the vascular tone of the great arteries (Vb) to (0.47 ± 0.06) U vs. (0.96 ± 0.14) U in the reference group, with a simultaneous decrease in the tone of the resistance arteries (Vm.n.) to (0.52 ± 0.08) U. The decreased tone of the resistance arteries, alongside with reduced blood filling of hepatic vessels, led to pathologic intrahepatic perfusion and the manifestations of the hepatocyte "deprivation" syndrome, which were among the major factors of the development of hepatic dysfunction. At the same time, one could observe decreased venous outflow, with the diastolic index dropping to (42.68 ± 2.10) U in the comparison group and (41.32 ± 1.12) U in the basic group vs. (56.52 ± 4.12) U in the reference group ($p < 0.05$).

4. Discussion of the research results. The above mentioned data suggest that uterine fibroids with concomitant hormonal and metabolic disorders deeply affect hepatic hemodynamics and decrease the blood supply of the liver as a result of pre- and postcapillary resistance [6, 7].

Alongside with cytolysis, cholestasis and hepatocellular insufficiency, the analysis of the obtained results of instrumental examinations of the livers of women affected by uterine fibroids reveals ultrasonographic signs of fatty hepatosis, disorders of the motor and evacuative function of the gallbladder and other disorders [8].

Rheohepatography is a rather simple and affordable method of diagnosing the severity of liver lesion in patients affected by uterine fibroids and enables the assessment of the degree of microcirculation disorders in the liver and its malfunction, which are characterized by capillary resistance to blood flow and desolation of capillaries as a result of the development of juxtacapillary circulation [9, 10].

Prospects of further research. Analysis of the recovery of the reproductive function and the incidence of reproductive losses in women affected by concomitant hepatobiliary diseases.

7. Conclusions.

1. Patients affected by uterine fibroids have preconditions for the development of functional disorders of hepatocytes as they present significant disorders of hepatic hemodynamics, decreased blood supply of the liver, as a result of pre- and postcapillary resistance.

2. The obtained results show that deep functional disorders of hepatocytes in women affected by uterine fibroids require pathogenetic correction by introducing drugs with hepatoprotective, antioxidant and angioprotective effects.

Conflict of interests: The authors confirm that there are no conflicts of interest.

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