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DOES THE ONCOLOGICAL RISK EXIST WHEN USING SILVER-CONTAINING INTRAUTERINE DEVICES?

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Abstract:

Aim. *The purpose of this study was to study the content of Barr's chromatin body and the characteristics of the mitotic regime of endometrial cells when using silver-containing intrauterine contraceptives for a different time period: from 6 months to 7 years.*

Materials and methods*. The study involved 160 healthy women, with an average age of 30 years (± 1,5). Endometrial scrapings were taken on the 8-10th or 19-23rd days of the menstrual cycle immediately after removal of silver-containing IUDs. For the study, cases were selected in which the uterine mucosa was without pathological changes. The control was the endometrium obtained in 30 women before the introduction of silver-containing IUD using the scratch biopsy (on the corresponding days of the cycle). For the study, cases were selected in which the uterine mucosa was without pathological changes. The control was the endometrium (scratch biopsy) obtained in 30 women before the introduction of silver-containing IUDs (on the corresponding days of the cycle). The mitotic regimen was studied on histological sections 6–9 μm thick, stained with Heidengain's iron hematoxylin.*

Results. *During the study it was found out that the content of Barr's chromatin did not undergo significant changes characteristic of proliferative processes of the uterine mucosa. Only in the group of women who used silver-containing IUDs for up to 1 year, the decrease in the mitotic activity of epithelial cells and endometrial stroma was detected, but it was transient. The analysis of the mitotic regime of epithelial and endometrial stroma cells with the use of silver-containing IUDs showed that the ratio of the number of prophases and metaphases, the number and spectrum of pathological mitoses did not differ significantly from the control group.*

Keywords: *silver-containing intrauterine contraceptive devices, Barr's chromatin, proliferative processes, mitotic regime, pathological mitoses.*

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INTRODUCTION:

Oncological diseases are associated with one of the most pressing problems of modern medicine. Malignant neoplasms take 2nd place in the general structure of causes of death worldwide. Along with the registered dynamics of increasing incidence, there is also an improvement in the methods of early diagnosis and screening, allowing to identify patients with precancerous diseases and the initial stages of malignant processes. Due to the wide spread of prolonged wearing of intrauterine contraceptives (IUDs) and the possibility of developing inflammatory and dystrophic changes [1,2,3,4], the oncological aspects of intrauterine contraception [5,6] attracted the researchers' attention [7,8].

Since the appearance of tumor tissue is always accompanied by a restructuring of the genetic apparatus, early changes in the form of biometric and histochemical changes in the cell nucleus are recorded first of all [9,10,11,12,13]. Therefore, the study of such changes can give objective tests to assess the risk of endometrial malignancy with prolonged intrauterine contraception

The purpose of this study was to study the content of Barr's chromatin body and the characteristics of the mitotic regime of endometrial cells when using silver-containing IUDs from 6 months to 7 years

MATERIALS AND METHODS:

The study involved 160 healthy women, with an average age of 30 years (± 1,5). Endometrial scrapings were taken on the 8-10th or 19-23rd days of the menstrual cycle immediately after removal of silver-containing IUDs. For the study, cases were selected in which the uterine mucosa was without pathological changes. The control was the endometrium obtained in 30 women before the introduction of silver-containing IUD using the scratch biopsy (on the corresponding days of the cycle). For the study, cases were selected in which the uterine mucosa was without pathological changes. The control was the endometrium (scratch biopsy) obtained in 30 women before the introduction of silver-containing IUDs (on the corresponding days of the cycle).

The mitotic regimen was studied on histological sections 6–9 μm thick, stained with Heidengain's iron hematoxylin. Mitotic activity was determined - the number of mitotically dividing cells per 100 fields of view of the microscope (field lens 90, eye lens 10), the percentage ratio of mitosis phases, the total number of pathological mitoses and the number of different forms of mitosis pathology, the total number of pathological mitoses and the number of different forms of karyokinesis pathology, expressed in percent of the total number of mitoses. Determination of Barr's chromatin body and its calculation were performed on histological sections with the Felgen reaction using a light microscope with magnification up to 1200 times. The number of epithelial cells containing Barr's chromatin body was counted in 2-3 sections of the slice with the removal of average values in percent. For this purpose, at least 300 cells in each section were studied. The data obtained were processed statistically using the Fisher LSD.

RESULTS AND DISCUSSION:

The results of the study showed that in the control group of patients on the 8-10th day of the cycle (middle stage of proliferation), the mitotic activity of the glandular epithelium was 51.2 ±1.8, stromal cells below 21.2 ±2.1. Among normal mitoses, prophases and metaphases prevailed (in the epithelium, respectively, 44.1% and 33.5%; in stromal cells, 46.2% and 35.1%). Similar data on the ratio of prophases and metaphases in endometrial cells were obtained by a number of researchers [14,15]. Pathological mitoses amounted to 2.0 ± 0.5% in the epithelium of the glands and 1.65 ± 0.1% in the stromal cells. Some forms of mitosis pathology were mainly represented by chromosome lag in metakinesis and chromosome separation, K-mitoses were often encountered; less commonly, bridges. The prevalence of these types of pathology of karyokinesis in the endometrium is also indicated by other authors [15,16].

On the 19-23rd day of the menstrual cycle (middle stage of secretion) in the control group of women, the mitotic activity of the epithelium was 15.8 ± 0.5, in the stroma - 4.7 ± 0.3. Profases and metaphases prevailed, with prophases being more common than metaphases. The number of pathological mitoses in this stage of the cycle tended to decrease, their spectrum was the same as in the proliferation phase.

As can be seen from table 1, with silver-containing intrauterine contraception, the mitotic activity of endometrial cells did not undergo significant changes. Only in the group of women who used silver-containing IUDs for up to 1 year, the decrease in the mitotic activity of epithelial cells and endometrial stroma was detected, but it was transient, and with the longer use of the IUDs, normal mitotic activity was noted. Similar results are reported by some researchers [14, 17], who studied the mitotic regime of the endometrium using IUDs. Since estrogens regulate DNA synthesis and the entry of cells into the mitosis phase, the decrease in the proliferative activity of endometrial cells when using inert IUDs during the year. L.S. Ezhova et al. [14] explain the violation of the utilization of steroid hormones in the cellular structures of target organs.

Table 1. Characterization of the mitotic regimen of the endometrium of women with different periods of use of silver-containing IUDs.

Mitotic regimen	Type of cells	Duration of use of silver-containing IUDs				
		control group	up to 12 months	13-36 months	37-60 months	61-84 months
The middle stage of proliferation						
Mitotic activity	epithelium	51,2±1,8	37,1±2,9*	53,2±1,4	49,1±1,8	52,2±3,5
	stroma	21,2±2,1	12,8±1,5*	23,0±3,1	22,0±1,3	23,9±2,4
The number of metaphases	epithelium	33,5±1,7;	34,0±3,8	38,9±3,45	31,2±1,1	37,8±2,4
	stroma	35,1±2,0	34,5±2,5	38,5±2,7	29,0±2,3	35,0±1,5
% pathological mitosis	epithelium	2.0 ± 0.5	1,8±0,5	1,97±0,15	1,55±0,3	2,3±0,7
	stroma	1,65±0,1	1,5±0,2	1,4±0,15	1,48±0,15	1,9±0,2
The middle stage of secretion						
Mitotic activity	epithelium	15.8 ± 0.5	15,2±0,45	15,2±0,4	15,5±0,3	15,5±0,3
	stroma	4.7 ± 0.3	3,4±0,5*	4,3±0,15	5,8±0,1	5,28±0,2
The number of metaphases	epithelium	24,9±1,7	23,0±2,45	27,0±5,6	31,1± 4,0	29,7±4,5*
	stroma	25,5±5,0	28,9±3,3	26,6±3,45	36,1±3,2	38,2±4,0
% pathological mitosis	epithelium	0,6±0,015	0,4±0,005*	0,6±0,15	0,6±0,04	0,5±0,015
	stroma	0,5±0,04	0,7±0,2	0,55±0,1	0,5±0,06	0,7±0,05*

*p<0,05.

At present, the great deal of factual material has been accumulated [15, etc.], which suggests that endometrial malignancy is accompanied not only by an increase in cell division intensity, but also by a sharp increase in the number of metaphases (up to 70%) and pathological mitoses (up to 40%).

The analysis of the mitotic regime of epithelial and endometrial stroma cells with the use of silver-containing IUDs showed that the ratio of the number of prophases and metaphases, the number and spectrum of pathological mitoses did not differ significantly from the control group. However, in our observation, patients using intrauterine contraceptives for more than 60 months showed the slight increase in the number of metaphases and pathological mitoses (p <0.05) with the predominance of the same types of pathology as in the control.

As the result of the study, it was found that the average content of Barr's chromatin body in the normal proliferating endometrium of the control group of women was 36.0 ± 2.3% in extreme cases from 22 to 57%, in the secretively transformed - 40.8 ± 1.5% in extreme cases from 28 to 65%.

Data on the average content of Barr's chromatin in the glandular epithelium of unchanged endometrium depending on the duration of use of silver-containing IUDs are presented in table 2, which shows that the content of Barr's chromatin did not undergo significant changes characteristic of proliferative processes of the uterine mucosa [18].

However, there was the increase in the content of Barr's chromatin in the endometrium of women who used silver-containing IUDs up to 12 months (p <0.05). The detected percentage increase in Barr's chromatin was combined with the decrease in the mitotic activity of the glandular epithelium of the endometrium. The decrease in the proliferative activity of the cells of the uterine mucosa during the use of silver-containing IUDs was transient.

Table 2. The content of Barr's chromatin activity of the endometrial glandular epithelium, depending on the duration of intramitotic activity of exact contraception

Duration of use of silver-containing IUDs	The middle stage of proliferation		The middle stage of secretion	
	number of women	Barr's chromatin content in %	number of women	Barr's chromatin content in %
Control group	15	36,1±2,2	17	42,0±1,45
6-12	15	50,0±1,5*	15	53,9±2,5*
13-36	17	33,1±1,6	15	44,2±1,3
37-60	15	35,8±1,7	16	40,3±1,4
61-84	15	34,1±2,0	15	39,1±1,8

*p<0,05.

CONCLUSION:

Thus, as the result of the study, it can be concluded that in the endometrium when using silver-containing intrauterine contraceptives, conditions are not created for the occurrence of pronounced proliferative processes and atypia.

List of symbols and Abbreviations
IUDs - intrauterine contraceptive devices

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