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ABOUT THE MECHANISM OF THE CONTRACEPTIVE ACTION OF SILVER-CONTAINING INTRAUTERINE DEVICES

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Abstract:

Aim. *The purpose of this study was to perform the histochemical study of the glycogen content in the endometrium of women using silver-containing intrauterine contraceptives for a different time period: from 6 months to 7 years.*

Materials and methods*. The mucous membrane of the uterus was studied in 94 healthy women aged 22–43 years in various phases of the menstrual cycle. The control group included 20 healthy women aged 22 years to 39 years who did not use IUDs during the examination, but later using this type of contraception. Endometrial biopsy was performed at various phases of the menstrual cycle. Glycogen was detected by the Shabadash method with the control treatment of sections of saliva amylase for 5 minutes. The histological examination of the endometrium was performed (stained with hematoxylin and eosin). Histochemical reactions to glycogen were quantified by the Astaldi method as modified by A. B. Pavlova et al.*

Results. *During the study it was found out that the revealed decrease in the amount of glycogen in the endometrial stroma in the secretory phase and the tendency to the accumulation of glycogen in the endometrium during the proliferative phase of the menstrual cycle when using silver-containing IUDs can be considered as the change in the functional state of the mucosa under the influence of the IUD.*

Keywords: *silver-containing intrauterine contraceptive devices, glycogen, mechanism of action, endometrium.*

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INTRODUCTION:

The problem of birth control is one of the most pressing problems of modern society [1,2,3]. Often circumstances are such that a woman temporarily cannot have children due to health reasons or due to some other reasons [4,5,6,7]. In addition, the experience of WHO shows that providing intervals between childbirths of at least 2-2.5 years, allows to reduce child mortality in childbirth by 4, and maternal - by 2 times [8]. One of the most common methods of contraception in our country is considered to be intrauterine contraceptives (IUDs). The authors are interested in various aspects of the use of IUDs [9,10,11,12,13].

When using IUDs, researchers found various pathological processes in the endometrium [14,15,16,17,18]. Human endometrial gland epithelial cells have the ability to secrete glycogen. Studying the content of glycogen in the endometrium allows us to judge the functional activity of the endometrium and the hormonal effects on it.

The content of glycogen in the endometrium in various phases of the menstrual cycle was studied by a number of authors [19,20,21,22,23,24], but the results of these studies are contradictory. There are no studies of glycogen in the endometrium when using silver-containing IUDs.

The purpose of this study was to perform the histochemical study of the glycogen content in the endometrium of women using silver-containing intrauterine contraceptives for a different time period: from 6 months to 7 years.

MATERIALS AND METHODS:

The mucous membrane of the uterus was studied in 94 healthy women aged 22–43 years in various phases of the menstrual cycle. **Up to 12 months, 11 women used silver-containing IUDs, up to 3 years - 18, up to 5 years - 25, up to 7 years - 20**. The control group included 20 healthy women aged 22 years to 39 years who did not use IUDs during the examination, but later using this type of contraception.

Endometrial biopsy was performed at various phases of the menstrual cycle. In the main group, endometrial biopsy with the microcurette or endometrial scraping was obtained in the presence of silver-containing IUD or immediately after its removal. The endometrium was fixed in the 10% solution of neutral formalin and, after appropriate histological processing, paraffin sections were prepared with the thickness of 6–9 μm.

Glycogen was detected by the Shabadash method with a control treatment of sections of saliva amylase for 5 minutes. In parallel with the histochemical, the histological examination of the endometrium was performed (stained with hematoxylin and eosin).

Histochemical reactions to glycogen were quantified by the Astaldi method as modified by A. B. Pavlova et al. The stain intensity of glycogen detected by the histochemical method was evaluated in 100 cells: intensive (+ + +), moderate (+ +), weak (+) staining, 0 - lack of staining. The average histochemical color index (AHCI) was determined as the quotient of dividing by 100 the product of the number of cells by the corresponding number of pluses of the staining intensity. The data obtained were processed statistically using the Fisher LSD.

RESULTS AND DISCUSSION:

In the control group of women, the proliferation phase was characterized by the low glycogen level both in the gland epithelial cells (AHCI = 1.0 ± 0.015) and in the stromal cells (AHCI = 0.49 ± 0.02) of the endometrium. From the 5th to the 10th day of the menstrual cycle, the glycogen gland epithelium cells contained little. At the proliferation stage (11-14th day) in the basal sections of the epithelial cells of most of the glands, glycogen appeared in the form of small granules. In the stroma, glycogen was determined in the insignificant amount in the cytoplasm of cells located near the glands. From the 16-17th to the 23-24th days of the menstrual cycle, large granules of glycogen were found, mainly in the apical parts of the cells of the endometrial glands, the apocrine nature of secretion was well traced (AHCI = 2.6 ± 0.025). Due to the high glycogen content in many cells, the nuclei were located at the basement membrane. By the end of the phase of secretion of the menstrual cycle, glycogen was determined predominantly outside the cells; there was no glycogen in the epithelium of most glands (AHCI = 0.1 ± 0.015). In the phase of secretion, glycogen was constantly detected in stromal cells, while its accumulation rate was lower than in epithelial cells (AHCI = 1.78 ± 0.015).

Thus, the determination of glycogen content in the endometrium of healthy women of childbearing age has shown that the intensity of its accumulation throughout the menstrual cycle is constantly changing and is determined by the effect of sex hormones.

In women who used silver-containing IUDs, on the 8-10th day of the menstrual cycle, glycogen in the glandular epithelium of the endometrium was found in the form of small granules, mainly in the apical part of the cells (AHCI = 1.25 ± 0.015; $p > 0.05$).

Glycogen granules were rarely found in stromal cells (AHCI = 0.52 ± 0.02; p> 0.05); in the glandular epithelium of the endometrium during the proliferative phase of the menstrual cycle, with the use of silver-containing IUDs, there was the tendency to glycogen accumulation.

In the phase of secretion, the glycogen content in the glands was approximately the same as in the control group (AHCI = 2.3 ± 0.01; p> 0.05). Glycogen was localized mainly in the apical part of the cells of the glandular epithelium of the endometrium. In stromal cells, glycogen was detected in the smaller amount compared to the control group (AHCI = 1.32 ± 0.02; p> 0.05).

Analysis of histochemical data depending on the period of use of silver-containing IUDs showed that the similar distribution of glycogen in the endometrium occurs during the first year after using the contraceptive and does not undergo significant changes in the future (with its longer use).

According to the data of L. A. Mozhukhina [25], the decrease in glycogen content in the endometrium can cause infertility and miscarriages. It can be assumed that the decrease in glycogen content in the stroma of the uterine mucosa in the secretory phase of the cycle that we detected is one of the contraceptive mechanisms of silver-containing IUDs. However, one should take into account the data of Huges and Csermely [26], who showed that the same glycogen content in the proliferative and secretory phases may indicate enhanced proliferation of endometrial cells.

THE RESULTS OF OUR RESEARCH:

as well as the data of B.I. Zheleznova et al. [27], V.I. Grishchenko et al. [28], Rosado et all [29], show that with the use of silver-containing IUDs in the secretory phase of the menstrual cycle, the accumulation of glycogen in the stroma of the endometrium decreases. This may indicate an increased consumption of glycogen due to increased metabolic processes in the endometrium in the presence of a contraceptive in the uterine cavity. It is known that the increase in glycogen content in the secretory phase of the cycle in the endometrium contributes to the nidation of a fertilized egg [30].

The histochemical study of endometrial trains in 22 women, 6 months after the removal of silver-containing IUDs, revealed that 16 of them had normal endometrial glycogen content. AHCI was 1.51 ± 0.015 in the glandular epithelium in the proliferation phase and 2.64 ± 0.025 in the secretion phase, in stromal cells, 0.52 ± 0.01 and 1.8 ± 0.015, respectively (when compared with the control group, p> 0 , 05).

CONCLUSION:

Thus, the revealed decrease in the amount of glycogen in the endometrial stroma in the secretory phase and the tendency to the accumulation of glycogen in the endometrium during the proliferative phase of the menstrual cycle when using silver-containing IUDs can be considered as the change in the functional state of the mucosa under the influence of the IUD. These data confirm the importance of the endometrial factor in achieving the contraceptive effect of inert IUDs.

List of symbols and Abbreviations
IUDs - intrauterine contraceptive devices
AHCI - average histochemical color index

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