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Research Article

**ENDOMETRY RESPONSE TO SILVER-CONTAINING
INTRAUTERINE DEVICES**¹Petrov Yu.A., ²Kupina A.D.

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¹ Doctor of Medicine, Professor, Department of Obstetrics and Gynecology № 2, Federal State Budgetary Educational Institution of Higher Education «Rostov State Medical University» of the Ministry of Healthcare of the Russian Federation, Rostov-on-Don, Russian Federation -mr.doktorpetrov@mail.ru²Clinical Resident of the Department of Obstetrics and Gynecology №2 Federal State Budgetary Educational Institution of Higher Education «Rostov State Medical University» of the Ministry of Healthcare of the Russian Federation, 344022, Rostov-on-Don, Russian Federation – anastasya1997@bk.ru**Article Received:** December 2019 **Accepted:** January 2020 **Published:** February 2020**Abstract:**

Aim. The purpose of this study was to study the structural and functional-morphological features of the endometrium against the background of prolonged intrauterine contraception and after it.

Materials and methods. Scrapes of the uterine mucosa were studied in 546 women aged 20-45 years who used inert IUDs for 3 months to 7 years. The control group consisted of 96 women. Endometrial biopsy with the microcurette was performed before the planned introduction of IUDs in this group.

Results. During the study it was revealed that 75% of women when using silver-containing IUDs had the normal endometrial condition. With prolonged continuous use of IUDs (more than 60 months), the increase in the frequency of pathological changes in the endometrium (chronic non-specific endometritis, focal stromal fibrosis, atrophic changes in the endometrium) was observed, which indicates a continuous presence of the contraceptive in the uterine cavity for no more than 5 years.

Keywords: silver-containing intrauterine contraceptive devices, menstrual cycle, endometrial reaction, chronic endometritis, hyperplasia.

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INTRODUCTION:

Family planning is the birth of only desired children in a convenient period of time for parents. One of the main methods of family planning is effective, harmless and comfortable contraception [1,2]. Contraception, being the method of family planning, can be simultaneously considered the way to prevent abortion and related complications [3,4]. The frequency of abortion complications in women of childbearing age reaches 30%, and among the pre-pregnant women this indicator is 45% [5].

Search and introduction into widespread practice of the most effective, harmless, long-acting contraceptives are gaining significant social and medical importance in the interests of maternal health and future offspring.

Recent studies have shown that one of the most common methods of pregnancy protection is the use of intrauterine contraceptives [6]. IUDs are widely distributed throughout the world; they are used by more than 100 million women in the world [7,8].

The use of intrauterine devices for contraception has been the subject of much research [9,6,10,11.]. However, the analysis of modern literature has shown that some clinical and morphological aspects of intrauterine contraception are still controversial and require further development. So, there is little systematic data regarding studies of the endometrium with prolonged intrauterine contraception (more than 5 years) and at various intervals after it. Unit studies devoted to the use of silver-containing IUDs.

In this regard, questions highlighting the effect of the prolonged use of silver-containing IUDs on the women's reproductive system [12,13], in particular on the uterine mucosa [14,15], are of great importance. According to literature data, the period of use of IUDs in most observations is 12-60 months [16, 17, 18,19].

The purpose of this study was to study the structural and functional-morphological features of the endometrium against the background of prolonged intrauterine contraception and after it.

MATERIALS AND METHODS:

Scrapes of the uterine mucosa were studied in 546 women aged 20-45 years who used inert IUDs for 3 months to 7 years. The control group consisted of 96 women. Endometrial biopsy with the microcurette was performed before the planned introduction of IUDs in this group. The data obtained were processed statistically using the Fisher LSD.

After fixation in the 10% solution of neutral formalin and the corresponding histological treatment, the endometrium was poured into paraffin. Sections were stained with hematoxylin-eosin and according to Van Gieson.

RESULTS AND DISCUSSION:

In 93% of patients, the contraceptive was withdrawn due to prolonged wearing or desire of a woman. Only 8% of women had clinical indications for removal of the IUD (menstrual irregularities, the onset or obstruction of the inflammatory process of the internal genital organs, severe pain, etc.).

Most women who used silver-containing IUDs did not show pathological changes in the endometrium. Inconsistency of the histological structure of the endometrium with the day of the menstrual cycle (mainly in the form of the lag of histofunctional changes in the endometrium by 2-9 days) was observed in 17% of women with the established phase of the menstrual cycle.

Fibroblastic transformation of the stroma in the surface layers of the endometrium was observed in 5,2% of women. Similar local changes in the uterine mucosa were found at different times of using the IUD, but more often when using the IUD for 5-7 years.

In 9.8% of patients, when using IUDs in the endometrium, cell infiltrates were noted. They were more often located in the stroma, less often periglandularly and perivascularly. The composition of infiltrates in 24 patients was represented by lymphocytes, in 14 patients by lymphocytes and leukocytes, in 7 by lymphocytes and histiocytes. Usually small focal infiltration was found, but diffuse infiltration was also detected. It should be noted that the nature of cell infiltration and its frequency did not depend on the duration of wearing IUDs and was usually not accompanied by clinical manifestations of endometritis. Focal stromal fibrosis and cellular infiltration of the endometrium were regarded as a kind of biological reaction of the body to the foreign object (IUDs).

In 7% of women, the endometrial pattern was assessed as chronic non-specific endometritis [20,21]. When making this diagnosis, we proceeded from the morphological criteria of chronic endometritis [22,23], which include inflammatory infiltrates, consisting mainly of lymphoid and plasma cells, as well as sclerotic changes in the vessels, fibrosis of the stroma, etc. Therefore, when using silver-containing IUDs in the glandular epithelium of the uterine mucosa, pathological proliferation of the endometrium is not observed, as well as when using indifferent plastic

contraceptives. As for the frequency of chronic endometritis when using IUDs, it was characterized by the slight increase compared with the initial data when using IUDs for 1-5 years, but raising with their longer use (5-7 years).

Minor atrophic changes in the endometrium were observed only in 0.4% of women using IUD. Hyperplastic processes of the endometrium on the background of intrauterine contraception were diagnosed in 4% of women. The frequency of glandular endometrial hyperplasia did not depend on the period of use of IUDs, but was slightly higher than in the control group (3.0%; $P > 0.05$). The study showed that in most cases, glandular endometrial hyperplasia was asymptomatic, often mixed (78%) (according to the classification of O. I. Topchieva [24]), less often proliferative. Atypical hyperplasia or endometrial cancer with the use of IUDs was not found in any case.

Comparison of the nature of the complications due to which it was necessary to remove IUDs with the histological picture of the endometrium showed that endometrial changes did not have constant clinical symptoms and were observed with various complications associated with the use of IUDs.

However, the frequency of pathological changes in the endometrium (63%) in case of complications of intrauterine contraception, which caused the extraction of IUDs, turned out to be significantly higher ($P < 0.05$) than with asymptomatic use (22%).

Changes in the uterine mucosa did not depend on the size of IUDs. With the use of IUDs immediately after artificial abortion, signs of chronic nonspecific endometritis and fibroblastic transformation of the stroma were noted in more cases (14%) than with the introduction of IUDs outside of abortion (11%; $P < 0.05$).

To clarify the possibility of the reverse development of pathological changes in endometrium with intrauterine contraception, the dynamic examination of women was performed 3-12 months after extraction of IUDs using cytological and histological methods (endometrial biopsy with the microcurette).

In 5 women who, at the time of contraceptive removal from the uterine cavity, lag of histofunctional endometrial transformations was noted, 3 months after the removal of the IUD, the endometrial pattern corresponded to the day of the menstrual cycle. 5 out of 6 women who were diagnosed with lymphocyte infiltration with the admixture of leukocytes and histiocytes when removing IUD in the uterine mucosa, did not have

such infiltration after 3-4 months. In 5 women, focal stromal fibrosis was detected in the endometrium when the IUD was removed, however, it was not determined 3-4 months after contraception in 4 women and was slightly expressed in 1 woman.

In 6 out of 12 women with chronic nonspecific endometritis detected at the time of extraction of the IUD, these changes regressed. In 3 patients, the normal state was noted, in 4 women dystrophic changes were revealed without pronounced signs of inflammation. 5 women half a year after the extraction of the IUD had unexpressed signs of chronic endometritis. Among 16 women who were diagnosed with glandular endometrial hyperplasia when removing the silver-containing intrauterine contraceptive, when examined 6 months after contraception, 8 of them had normal endometrium, 3 of them showed dystrophic changes in the endometrium, and 2 women had focal proliferation of the endometrial glands. 7 women with identified glandular hyperplasia of the mucous membrane after stopping intrauterine contraception as the contraceptive and therapeutic agent were prescribed combined oral contraceptives with a low hormone content. Subsequent cytohistological control after 4-5 months, glandular hyperplasia was not determined in any case. Consequently, the detected endometrial hyperplastic processes in women with silver-containing IUDs were not persistent.

CONCLUSION:

1. Thus, our data indicate that 75% of women when using silver-containing IUDs had the normal endometrial condition. With prolonged continuous use of IUDs (more than 60 months), the increase in the frequency of pathological changes in the endometrium (chronic non-specific endometritis, focal stromal fibrosis, atrophic changes in the endometrium) was observed, which indicates a continuous presence of the contraceptive in the uterine cavity for no more than 5 years. Similar patterns in the endometrium were found with the use of indifferent IUDs, however, inflammatory changes in the endometrium were detected less frequently, already at the very shortest time of using the silver-containing contraceptive.

2. Clinical and morphological examination confirms that with intrauterine contraception, clinical symptoms are nonspecific and do not reflect the depth of morphological changes in endometrium. In the event of complications that are not amenable to conservative treatment, removal of the IUD is indicated regardless of the duration of intrauterine contraception.

3. Re-use of IUDs if a woman wants it and there are no contraindications is recommended no earlier than 3-5 months, since during this time changes in the endometrium against the

background of intrauterine contraception disappear or undergo significant regression.

List of symbols and Abbreviations

IUDs - intrauterine contraceptive devices

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