



CODEN [USA]: IAJPBB

ISSN: 2349-7750

INDO AMERICAN JOURNAL OF  
**PHARMACEUTICAL SCIENCES**

<http://doi.org/10.5281/zenodo.3824761>

Available online at: <http://www.iajps.com>

Research Article

## SILVER-CONTAINING INTRAUTERINE DEVICES AND HYPERPLASTIC CHANGES OF ENDOMETRIUM

<sup>1</sup>Petrov Yu.A and <sup>2</sup>Kupina A.D.

FGBOU VO «Rostov State Medical University» of the Ministry of Health of the Russian Federation, 344022, Rostov-on-Don, Russia.

<sup>1</sup> 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.ru

<sup>2</sup>Clinical 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:** March 2020

**Accepted:** April 2020

**Published:** May 2020

**Abstract:**

**Aim.** The purpose of this study was to study the frequency and features of endometrial hyperplastic processes, endo- and ectocervix in women using silver-containing IUDs for a different period of time: from 3 months to 7 years.

**Materials and methods.** The study involved 450 women who used silver-containing IUDs from 3 months to 7 years. The histological examination of scrapings was performed, as well as the cytological examination of smears from the cervix and the lower third of the cervical canal. The control group consisted of 270 patients (not using contraception) aged 21–45 years who underwent colpositological examination, 65 of them underwent scratch biopsy (before installing silver-containing IUDs). Histological sections were stained with hematoxylin and eosin (Felgen), cytological preparations were stained with azure-eosin. The content of Barr's chromatin body and the features of the mitotic regime of glandular epithelial cells were studied and compared with normal endometrial cells of the middle proliferation stage. Barr's chromatin body counting was performed in slices with the Felgen's reaction with the increase of up to 1200 times.

**Results.** During the study it was found out that silver-containing IUDs did not increase the frequency of precancerous processes and cervical cancer and did not lead to the development of endometrial cancer. In addition, some features of the proliferative processes of the mucous membrane of the body and cervix were established in women with silver-containing IUDs.

**Keywords:** silver-containing intrauterine contraceptive devices, hyperplastic processes, mitotic regime, ectocervix, endocervix.

**Corresponding author:**

**Kupina Anastasia Dmitrievna,**

Clinical Resident,

Federal State Budgetary Educational Institution of Higher Education  
«Rostov State Medical University» of the Ministry of Healthcare of the  
Russian Federation, 344022, Russian Federation, Rostov region,  
Rostov-on-Don, 29 Nakhichevan lane.

Phone: 89518268150, E-mail: [anastasya1997@bk.ru](mailto:anastasya1997@bk.ru)

QR code



Please cite this article in press Petrov Yu.A and Kupina A.D, *Silver-Containing Intrauterine Devices And Hyperplastic Changes Of Endometrium.*, Indo Am. J. P. Sci, 2020; 07(05).

## INTRODUCTION:

Oncological diseases are one of the most important problems in the modern world. Firstly, this is due to an increase in the number of patients. Secondly, with high mortality in the later stages. In women, the most common malignant neoplasms are breast cancer and uterine cancer [1,2,3].

Among modern methods of preventing pregnancy, intrauterine devices (IUDs) are widely used [4,5,6,7]. This method of contraception is easy to use, convenient, highly effective and cost-effective. It was also found that IUDs rarely cause complications during use [8,9,10,11]. However, the question of the possibility of the occurrence of precancerous processes and cancer of the mucous membrane of the body and cervix of the uterus when using IUD is still a moot point. [12,13,14,15,16]

**The purpose of this study** was to study the frequency and features of endometrial hyperplastic processes, endo- and ectocervix in women using silver-containing IUDs for a different period of time: from 3 months to 7 years.

## MATERIALS AND METHODS:

The study involved 450 women who used silver-containing IUDs from 3 months to 7 years. The histological examination of scrapings was performed, as well as the cytological examination of smears from the cervix and the lower third of the cervical canal. The control group consisted of 270 patients (not using contraception) aged 21–45 years who underwent colposcopic examination, 65 of them underwent scratch biopsy (before installing silver-containing IUDs).

Histological sections were stained with hematoxylin and eosin (Felgen), cytological preparations were stained with azure-eosin. For the purpose of the comprehensive assessment of the identified endometrial hyperplastic processes, the content of Barr's chromatin body and the features of the mitotic regime of glandular epithelial cells were studied and compared with normal endometrial cells of the middle proliferation stage. The mitotic index was determined (the number of mitotically dividing cells per 1000 cells; field lens 90, eye lens 10), the percentage of mitosis phases, the total number of pathological mitoses and the number of different forms of karyokinesis pathology, expressed as a percentage of the total number of mitoses.

Barr's chromatin body counting was performed in slices with the Felgen's reaction with the increase of 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 derivation 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 indicate the absence of malignant growth in the endometrium of women using silver-containing IUDs. Hyperplastic processes were detected in 17 patients ( $3.2 \pm 0.5\%$ , in the control  $2.0 \pm 0.8\%$ ,  $p > 0.05$ ) aged 24–41 years. In 15% of cases, there were medical indications for the removal of silver-containing IUDs (mainly due to menstrual irregularities in the type of hyperpolymenorrhea), in other women, silver-containing IUDs were removed at their request or due to prolonged use of a contraceptive. The frequency of glandular endometrial hyperplasia was independent of the duration of intrauterine contraception.

In 14 out of 17 women, hyperplastic processes were characterized by diversity in the structure of the endometrial glands and their epithelium. In approximately equal amounts, proliferating and secreting cells were found in it. The "proliferative uterine" epithelium (according to the classification of Kostina LI) lined small rounded glandular. The lumens of the glands lined with "secretory-uterine" epithelium are expanded more, irregularly shaped. Such the histological picture is estimated by researchers as the mixed form of glandular hyperplasia. In 4 cases, the proliferative form of glandular hyperplasia was detected.

The mitotic index for glandular hyperplasia was approximately the same as in the control group ( $p > 0.05$ ). But the number of metaphases ( $p < 0.05$ ) and pathological mitoses ( $p < 0.05$ ) increased. The spectrum of pathological mitoses did not significantly change with respect to the control data. The average content of Barr's chromatin body in the glandular epithelium with detected hyperplastic processes was  $25.2 \pm 1.3\%$  ( $34.0 \pm 2.2\%$  in the control,  $p < 0.05$ ).

Cytohistological examination of the endometrium was performed on 10 women 6-12 months after extraction of silver-containing IUDs. 6 of them showed no signs of hyperplasia. Another 7 patients for therapeutic purposes were prescribed synthetic progestins according to the contraceptive regimen. With subsequent cytohistological control after 3-4 months and with further observation during the year, endometrial hyperplastic processes in these women were not detected.

**Table 1. Mitotic regime of glandular epithelium in endometrial hyperplastic processes in women using silver-containing IUDs.**

Endometrial condition	Number of observations	Mitotic index, %	% mitosis phase ratio				% pathological mitosis	% different forms of pathological mitoses					
			prophase	metaphase	anaphase	telophase		1	2	3	4	5	6
Normal endometrium	8	8,9±1,2	40,5	31,8±1,7	7,1	17,9	2,0±0,15	0,9	0,3		0,2		0,4
Hyperplastic endometrium	10	8,2±1,5	24,8	56,5±1,3*	5,6	11,7	7,3±1,0*	2,5	1,4	0,5	0,1	0,2	2,9

1-lagging of chromosomes and their fragments in metakinesis; 2-lagging of chromosomes and their fragments at discrepancy; 3-chromosome bridge; 4-three-group metaphase; 5-multipolar mitosis; 6-K mitosis.

\*p<0,05.

Thus, glandular hyperplasia of the uterine mucosa, diagnosed with the use of silver-containing IUDs, had some features. Hyperplasia in most cases was of the mixed form, was often transient, and responded well to synthetic progestin therapy. The data obtained by us coincide with the results of other authors [17,18]. Changes in the mitotic regimen and a decrease in the level of Barr's chromatin body during the diagnosed hyperplastic processes were moderately expressed, while pre-cancerous changes in the endometrium are characterized by significant violations of the mitotic regimen and a sharper decrease in the Barr's chromatin body's level [19,20,21].

In 10 cases ( $2.2 \pm 0.3\%$ , in the control  $0.6 \pm 0.15\%$ ;  $p < 0.05$ ), hyperplastic changes in the endocervical epithelium were noted. However, proliferation was without signs of atypia, which was further proved by histological examination of endocervix scrapings. The frequency of the hyperplastic processes of the endocervical epithelium increased by 2-3 times when using silver-containing IUDs for 7 years ( $5.9 \pm 0.5\%$ ,  $p < 0.05$ ). During dynamic cytological control after extraction of silver-containing IUDs, hyperplastic changes in the cervical epithelium were not detected in most cases.

In 8 patients ( $1.9 \pm 0.3\%$ , in the control  $1.7 \pm 0.3\%$ ,  $p > 0.05$ ), cytograms from the cervix uteri showed flat epithelial dysplasia, in 2 cases they were moderately expressed, in 6 - poorly expressed. The cytological diagnosis is confirmed by histological examination of biopsy specimens. Re-examination of these women was carried out every 3 months. The progression of the process was not detected in any observation. In 6 women, the intrauterine contraceptive was removed; upon subsequent cytological examination within a year after removal of silver-containing IUDs, in 5 cases dysplasia underwent regression, in 3 remained stable. Therefore, in women with silver-containing IUDs,

cervical dysplasia of the cervix was mainly mild and not persistent.

In 1 woman ( $0.2 \pm 0.01\%$ , in the control  $0.15 \pm 0.01\%$ ,  $p > 0.05$ ) 32 years later, after 6 years of using silver-containing IUD, intraepithelial cervical cancer was diagnosed.

#### CONCLUSION:

Thus, the study showed that silver-containing IUDs did not increase the frequency of precancerous processes and cervical cancer and did not lead to the development of endometrial cancer. In addition, some features of the proliferative processes of the mucous membrane of the body and cervix were established in women with silver-containing IUDs. The identification in some women of hyperplastic changes in the endometrium and endocervix, as well as ectocervix dysplasia, justifies the need for regular clinical and cytological examination of patients using silver-containing intrauterine contraceptives and afterwards.

#### List of symbols and Abbreviations

IUDs - intrauterine contraceptive devices

#### REFERENCES:

1. Felix AS, Gaudet MM, Carlo La Vecchia CL et al. Intrauterine devices and endometrial cancer risk: a pooled analysis of the Epidemiology of Endometrial Cancer Consortium. *Int J Cancer*. 2015 Mar 1; 136(5): E410–E422.
2. Petrov YuA, Kovaleva EA. The valid duration of use plastic intrauterine contraceptives. *Obstetrics and Gynecology*, 1986; 7: 40.
3. Nelson AL, Massoudi N. New developments in intrauterine device use: focus on the US. *Open Access J Contracept*. 2016; 7: 127–141.
4. Petrov YuA, Kovaleva EA. Features of colpocytograms of women using intrauterine contraception. *Klinicheskaya Laboratornaya Diagnostika*, 1986;1: 51-52.

5. Kupina AD, Petrov YuA. Efficiency of sonographic research in diagnostics of chronic endometritis. *Indo American Journal of Pharmaceutical Sciences*, 2019; 6(11):15210-15213.
6. Petrov YuA, Dolzhenkova LM. Histochemical examination of glycogen in the endometrium of women using intrauterine contraceptives. *Obstetrics and Gynecology*, 1985;9:57-58.
7. Petrov YuA, Rymashevsky NV, Pavlova AP. Inflammatory diseases of the pelvic organs with intrauterine contraception. *Problems of maternity and child care*, 1990;11: 57-59.
8. Radzinsky VE, Kostin IN, Polina ML, Petrov YuA, Gasanova BM. Diagnostic significance of chronic endometritis macrotypes differentiation among women with reproductive losses. *Gynecological Endocrinology*, 2017; 33(1): 36-40.
9. Petrov YuA. The content of DNA in the cells of the endometrial glands with the use of intrauterine contraceptives. *Problems of maternity and child care*, 1984;7: 64.
10. Petrov YuA, Rymashevsky NV, Kovaleva EA. Endometrial condition with intrauterine contraception. *Problems of maternity and child care*, 1988;3:59-62.
11. Petrov YuA, Kovaleva EA. Proliferative mucosal changes of the corpus and cervix uteri in women using intrauterine contraceptives. *Problems in oncology*. 1986; 32: 49-52.
12. Petrov YuA, Rymashevsky NV, Kovaleva EA. The effect of intrauterine contraceptives on the mucous membrane of the cervical canal and cervix. *Problems of maternity and child care*, 1987;8:59-61.
13. Whiteman MK, Zapata LB, Tepper NK. Use of contraceptive methods among women with endometrial hyperplasia: a systematic review. *Contraception an international reproductive health journal*, 2010; 82(1): 56-63.
14. Petrov YuA., Kupina AD. Features of the mitotic regime of endometrial cells against the background of the use of silver-containing intrauterine devices. *Indo American Journal of Pharmaceutical Sciences*. 2020; 7(2):343-346.
15. Petrov YuA., Kupina AD. The response of the endometrium to intrauterine devices silver. *Indo American Journal of Pharmaceutical Sciences*. 2020; 7(2): 645-648.
16. Petrov YuA., Kupina AD. Cytomorphological study of endo- and ectocervix in patients with silver-containing intrauterine devices. *Indo American Journal of Pharmaceutical Sciences*. 2020; 7(3): 432-435.
17. Pisetsky DS, Spencer DM. Effects of Progesterone and Estradiol Sex Hormones on the Release of Microparticles by RAW 264.7 Macrophages Stimulated by Poly(I:C). *Clinical and vaccine immunology*, 2011; 18(9):1420–1426.
18. Rotkina I.E., Lutsik L.A. The effect of synthetic progestins on the content of sexual chromitotic activity of the hyperplastic endometrium. *Obstetrics and gynecology*. 1987; (7): 33-35.
19. Petrov YuA. Features of hyperplastic processes of the uterine mucosa in women using intrauterine contraceptives. *Problems of maternity and child care*, 1985; 11:67.
20. Yezhova LS, Zheleznov BI, Antipov NB. The effect of intramitotic activity of precise contraceptives on the mitotic regime of the endometrium. *Obstetrics and gynecology*. 1990; (3): 39-40.
21. Petrov YuA. Oncological risk assessment of intrauterine contraception based on cytological studies of the endometrium. *Problems in oncology*, 1985;12:53-56.