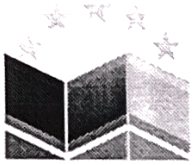

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Editorial office: Křižikova 384/101 Karlin, 186 00 Praha

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Лоскутова Т.А.,
Днепропетровский государственный медицинский университет,
Кафедра акушерства и гинекологии,
Доктор медицинских наук, Профессор
Грищенко А.С.
Днепропетровский государственный медицинский университет,
врач-интерн акушер-гинеколог

ASSESSMENT OF RISK FACTORS OF CHRONIC ENDOMETRITIS IN WOMEN WITH OF INTRAUTERINE INTERVENTIONS IN ANAMNESIS

Loskutova T.,
Dnipro State Medical University, obstetrics and gynecology department,
Doctor of Medical Science, Professor
Hryshchenko A.
Dnipro State Medical University, doctor intern obstetrician-gynecologist

АННОТАЦИЯ

В статье представлены результаты исследования по определению факторов риска формирования хронического эндометрита у женщин репродуктивного возраста. Установлено, что «слепое» фракционное выскабливание и медицинские аборты значительно увеличивают шансы развития хронического эндометрита в будущем. Никакой связи с наличием гистероскопии в анамнезе и последующим развитием ХЭ не установлено. По данным исследования доля ХЭ у пациенток с инвазивными вмешательствами в полость матки в анамнезе по данным иммуногистохимического определения маркера CD 138 составляет 78,4% против 7,7%, а по данным гистероскопического исследования 92,2% против 10,3% женщин без вмешательств в анамнезе

ABSTRACT

The article presents the results of a study of the determinetion the risk factors for the formation of chronic endometritis in women of childbearing age. It has been established that "blind" fractional scraping and medical abortions significantly increase the chances of developing chronic endometritis in the future. No association with hysteroscopic history and subsequent development of CE has been determined. According to the study, the proportion of CE in patients with a history of invasive interventions in the uterine cavity according to the immunohistochemical determination of the marker CD 138 is 78.4% vs. 7.7%, and according to hysteroscopic studies 92.2% vs. 10.3% of women without a history of intervention.

Ключевые слова: хронический эндометит, факторы риска, хирургические вмешательства в полость матки, бесплодие, гистероскопия, CD 138, инфекции передающиеся половым путем.

Keywords: chronic endometritis, risk factors, surgical intrauterine interventions, infertility, hysteroscopy, CD 138, sexually transmitted diseases.

Along with the high incidence of chronic inflammatory diseases of the cervix, vagina, uterine appendages, the incidence of chronic endometritis (CE) has recently increased. Chronic inflammation in the uterine mucosa is the cause of impaired women fertility, reproductive loss, abnormal uterine bleeding (AUB). CE is very common among women with idiopathic infertility (40.7 - 55.7%), unsuccessful IVF attempts (13.95 - 57.55%) and early pregnancy loss (42.9 - 56%) [1-6].

Chronic endometritis is most common in women with habitual miscarriage, as the prolonged persistence of infection in the endometrium, which is observed in CE, even in the absence of severe clinical manifestations of the disease, leads damaging of the receptor apparatus, which can cause reproductive dysfunction.

Chronic endometritis (CE) is a persistent inflammatory disease of the endometrial mucosa characterised by superficial endometrial edema, high stromal cell density, dissociated maturation between the epithelium and stroma, and endometrial infiltration by stromal plasma cells [7-8]. Risk factors for CE include surgery and intervention in the uterine cavity (cesarean section, diagnostic scraping of the uterine cavity) and foreign bodies in the uterine cavity (spiral, remnants of the fertilized egg), but sometimes the cause is unknown.

Long-term inflammatory process in the body stimulates the immune system, which leads to the formation of autoimmune responses that cause secondary damage, including endometrial hormone receptors, such as estrogen and progesterone. As a result, the endome-

trium becomes insensitive to hormonal influences, becomes thin, and, eventually, there is a defective transformation and unwillingness to accept the embryo.

Moreover, this affects the qualitative and quantitative changes in the endometrial microbiome and causes abnormal reproduction of various types of microorganisms, mainly gram-negative and intracellular bacteria (for example - Enterococcus faecalis, Mycoplasma, Ureaplasma, Escherichia coli. and Streptococcus spp.) [9,10]. As evidence of the infectious etiology of CE, several studies have found that specific cycles of antibiotics can cure CE in most patients [1,4,7].

In the majority of cases, CE in women is asymptomatic or patients have mild disorders such as abnormal uterine bleeding (AUB), dyspareunia, pelvic discomfort and leukorrhea [1,11,12]. In addition, CE cannot be identified by ultrasound due to the lack of specific ultrasound markers [2]. For these reasons, CE often goes unnoticed or is diagnosed accidentally during hysteroscopic treatment of gynecological diseases: AUB, polyps, endometrial hyperplasia, infertility or chronic pelvic pain [3]. Fluid hysteroscopy plays a central role in the diagnosis of CE. This technique allows to visualize the condition of the endometrium and identify changes that are specific to CE, namely: focal or diffuse micropolyps, stromal edema, focal hyperemia and hemorrhagic spots in the endometrium [3]. "

The current "gold" standard for the diagnosis of CE is endometrial biopsy with histological and immunohistochemical examination , which is held on 7-11 days of menstrual cycle (during this period the content of immunocompetent cells in the endometrium is minimal), that allows to identify plasma cells (CD138), which are the main diagnostic marker of chronic endometritis [1].

Despite the introduction of the latest diagnostic technologies and treatments, the incidence of CE is not reduced, which necessitates the prevention and detection of risk factors for chronic endometritis in women of childbearing age.

The purpose of the study was to determine the risk factors for the formation of chronic endometritis in women of childbearing age.

METHODOLOGY AND RESEARCH METHODS

90 patients were included in a prospective case-control study. The main (O) group consisted of 51 patients with a history of surgery (scraping, hysteroscopy or IUD – intrauterine device) in the uterine cavity. The control group (K) was formed by 39 women without surgery in the uterine cavity in the past. Also, the criteria for inclusion in the study were: age of patients 20-45 years, diagnosis of endometrial polyp, endometrial hyperplasia, abnormal uterine bleeding, female infertility, which were the basis for their hysteroscopy or hysteroresectoscopy. The study lasted from August 2020 to November 2021. It was approved by the Bioethics Commission.

All patients gave written consent for the anonymous use of their clinical data for research purposes.

To achieve the goal of the study were used the following methods: study of personal details, complaints, medical history and disease, general clinical and gynecological examination, histopathological examination, pathomorphological (histological, morphometric, immunohistochemical), statistical methods.

The comprehensive examination included anamnesis data, general clinical and gynecological examinations, laboratory and instrumental methods.

The diagnosis of CE was verified by hysteroscopy and immuno-histochemical examination of the endometrium (IHC). For endometrial IHC was used indirect streptavidin peroxidase method which is based on the detection of CD138 expression by Kit monoclonal antibodies. Monoclonal antibodies manufactured by Thermo Fisher Anatomical Pathology (Great Britain) CD138 Ab-2 (Clone MI 15) - a marker of plasma cells which were used as primary antibodies. The results of the reactions for each parameter were evaluated by the percentage of stained cells (nuclei) of a certain type by counting 100 cells of this type.

Hysteroscopic intervention was performed on 7-11 day of the menstrual cycle (MC) using Karl Storz equipment (Germany) with 7.5 mm optics and a viewing angle of 30 degrees according to the generally accepted method. Sterile irrigation solution "Turusol" was used as an optical medium. During hysteroscopy, the size and shape of the uterine cavity, the presence of deformities, endometrioid passages were assessed. The color, uniformity of color, folding and heterogeneity of the thickness of the endometrium, the presence of hemorrhages, polyp-like formations, intrauterine synechiae, foreign antibodies in the uterine cavity were evaluated Signs of CE were diffuse hyperemia, micropolyps, stroma edema.

Sonographic examination was performed in patients of all groups using series of longitudinal and cross sections using an ultrasound device Voluson E8 using a multi-frequency transvaginal transducer with a frequency of 4.0-7.5 MHz and, if necessary, abdominal, with a frequency of 3.5 MHz. The study was performed on the 5th-9th day of the menstrual cycle.

Statistical analysis of the results of the study was performed using licensed computer programs Microsoft Excel 2010 and Graph Pad Prism 5 (license number 35B73650-6899-11DA-6784-00232A9018BE).

The main characteristics are presented in the form of the number of observations (n), the arithmetic mean (M), the standard error of the mean (± m), relative values (abs.,%), The level of statistical significance (p). The normality of the distribution of quantitative traits was assessed using the Shapiro-Wilk and Kolmogorov-Smirnov criteria. Comparison of statistical characteristics in groups was performed using parametric and non-parametric criteria: estimation of probability of differences of averages for unrelated samples - by Student's criteria (t), probability of differences of qualitative indicators - by Pearson's Chi-square criterion ($\chi 2$), including correction Yates (Yates corrected), Fisher's exact test.The discrepancy was considered significant at $p < 0.05$.

RESULTS OF THE RESEARCH

The mean age of the studied women was 30.8 ± 4.2 years. Studied clinical groups did not differ significantly in age, body mass index, and duration of follow-up (p> 0.05). In the structure of morbidity, which became the basis for hysteroscopy, the indicators of the study groups did not differ and were: in the O group of endometrial polyps 20 (39.2%), in K - 15 (38.5%) patients, endometrial hyperplasia 12 (23,5%) and 10 (25.6%), accordingly, AUB 5 (9.8%) and 4 (10.3%), infertility 14 (27.4%) and 10 (25.6%) p > 0,05).

In the analysis of reproductive history it was found that 38 (74.5%) women in the main group had a history of childbirth, in K 25 (64.1%) (p> 0.05).12 (23.5%) women in group O had a history of sexually transmitted diseases and 2 (5.1%) in group K ($\chi 2 = 4.38$, p <0.05, OR = 5.69, 95 % CI 1.19-27.1).

The presence of any surgical intervention in the uterine cavity in the anamnesis was the main criterion for exclusion from the control group. Women of the main group had fractional diagnostic scraping for endometrial polyp, endometrial hyperplasia or AUB 23 (46,9%) (K=0, χ^2 =21,31, p<0,001, OR=65,1, 95% CI 3,8-1117,4), hysteroscopy 5 (9,8%) (K=0, p>0,05), medical abortion 26 (51%) (K=0, χ^2 =25,53, p<0,001, OR=82,1, 95% CI 4,8-1407,7), 12 (23,5%) used intrauterine devise (K=0, χ^2 =25,00, p<0,05, OR = 25,0, 95% CI 1,43-436,9)

During hysteroscopy, most of the 47 patients (92.2%) of the main group had hysteroscopic signs of chronic endometritis, which was significantly different from control group 6 (10.3%) ($\chi 2 = 50.68$, p <0.001, OR = 64,6 95% CI 15.1-195.8). The most common signs of inflammation in the endometrium were: focal hyperemia with a white central point, which were either localized or scattered in the endometrial cavity (strawberry symptom) in 40 (78.4%) in group O and 2 (5.1%) in K group ($\chi 2 = 44.8$, p <0.001, OR = 67.3 95% CI 12.5-222.5), the presence of plaques in 33 (64.7%) and 0 (0%), respectively (p <0.001), uneven thickness of the endometrium in 28 (54.9%) and (0%) (p <0.001), uneven color of the mucous membrane 18 (35.3%) and 4 (10.3%) ($\chi 2 = 6.21$, p <0.05, OR = 4.77 95% CI 1.4-13.5), mucosal hyperemia 20 (39.2%) and 3 (7.7%), ($\chi 2 = 7.43$, p <0.05, OR = 5.3 95% CI 1.5-14.9) polypoid formations 13 (25.5%) and 2 (5.1%) ($\chi 2 = 5.2$, p <0.05, OR = 6.33 95% CI 1.3-21.8), focal mucosal hypertrophy 7 (13.7%) and 1 (2.6%), punctate hemorrhages 5 (9.8%). Thinning of the mucous membrane was in every third patient of the main group - 15 (29.4%).

During the immunohistochemical reaction CD 138 was detected in 40 (78.4%) patients of the main group and in 3 (7.7%) in the control group, which confirmed the presence of classical CE in them (p <0.001, OR = 43.64 95 % CI 11.27-168.9). The density of CD 138 in the main group was 15.2 ± 2.3%, in the control - 10.1 ± 1.3% (p> 0.05).

Immunohistochemical determination of CD 138 confirmed the presence of CE in 85.1% of patients in the main group, where the diagnosis of chronic endometritis was determined on the basis of hysteroscopic examination, and in 50% of the control group. This means that hysteroscopic identification of CE at the premorphological stage demonstrates the high diagnostic specificity of this method.

CONCLUSIONS:

1. It is established that surgical interventions in the uterine cavity are the main cause of chronic endometritis. According to the study, the proportion of CE in patients with a history of invasive interventions in the uterine cavity according to the immunohistochemical determination of the marker CD 138 is 78.4% vs. 7.7%, and according to hysteroscopic studies 92.2% vs. 10.3% of women without a history of intervention.

2. It has been determined that "blind" fractional scraping and medical abortions significantly increase the chances of developing chronic endometritis in the future. No association with hysteroscopic history and subsequent development of CE has been established.

3. Sexually transmitted diseases almost 6 times increase the chances of developing chronic endometritis in the future (p <0.05, OR = 5.69, 95% CI 1.19-27.1)

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