CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
SJIF Impact Factor: 7.187

Online at: www.iajps.com Research Article

IMPAIRED IMMUNOREACTIVITY IN PATIENTS WITH CHRONIC ENDOMETRITIS

[1]Petrov Yu.A and [2]Kupina A.D.

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

[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.ru

[2]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 2021 **Accepted:** March 2021 **Published:** April 2021

Abstract:

Aim. *To determine changes in the body's immunoreactivity for each macrotype of chronic endometritis (CE), as well as determination of microbiological characteristics, alpha-2-microglobulin in blood serum*

Materials and methods*. Microbiological research and diagnosis of deoxyribonucleic acid of possible pathogens of CE, determination of embiotropic autoantibodies in blood serum (ELI-P-test), determination of the content of alpha-2-microglobulin (AMGF) in menstrual blood, sonographic, hysteroscopic and pathomorphological studies (aspirates and biopsies from the cervical canal and uterus).*

Results. *The results of the data showed that pathological changes in the body's immunoreactivity with each macrotype of chronic endometritis, as well as the determination of microbiological features, alpha-2-microglobulin in the blood serum are prognostic indicators of structural and functional changes in the endometrium in various types of chronic endometritis*

Keywords: *chronic endometritis, alpha-2-microglobulin, immunoreactivity, diagnostics.*

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

QR code

Please cite this article in press Petrov Yu.A and Kupina A.D., ***Impaired Immunoreactivity In Patients With Chronic Endometritis.,*** *Indo Am. J. P. Sci, 2021; 08(04).*

INTRODUCTION:

Preserving a woman's reproductive health and ensuring the birth of a healthy child are among the urgent tasks of modern medicine, which is confirmed in the program documents of the World Health Organization. One of the factors leading to a violation of a woman's reproductive health is chronic endometritis (CE) [1,2,3,4]. Medical and social significance of the problem of chronic endometritis and does not lose its relevance. This is due to the fact that damage to the endometrium in chronic endometritis is one of the reasons for infertility, miscarriage, ineffective use of assisted reproductive technologies [5,6]. Although chronic endometritis, as a separate nosological form, was first identified in the International Statistical Classification of Diseases, Injuries and Causes of Death IX revision in 1975 [7,8].

In modern research chronic endometritis quite often is considered as an autoimmune, microbial process. Immune deficiency is an important pathogenetic factor contributing to the development of endometrial inflammation against the background of maladjustment of the immune system, secondary immune deficiency, which reduces the body's resistance to infection [9,10,11]. Chronic endometritis is certainly a microbial or microbial-viral disease. Viral infection is detected in 49% of women and plays a large role in the disruption of the functional state of the endometrium and complicated course [12,13,14]. The concept of modern research focuses on understanding how to develop personal bacterial communities of the body, e.g. intestines, respiratory system, skin, vagina, etc. predispose to the onset of diseases or maintain a healthy state of the macroorganism [15,16].

Until recently, it was believed that the colonization of the upper genital tract by microbes is due exclusively to the pathological ascent of microorganisms from the vagina through the cervical canal [17,18,19,20]. With the advent of genetic methods for the determination and identification of bacteria (sequencing of the 16B rRNA gene), it became clear that the female reproductive system is not sterile, including the uterine cavity. There is a specific uterine microbiome that can affect reproductive function when the balance with the woman's immune system is imbalanced [21,22,23,24,25]. For a woman's health, the vaginal microbiome is important, which contains about 10% of the female microbiota and plays an exceptional role in maintaining the physiological norm of the genitourinary tract, preventing the development of pathological changes in it [26,27,28,29]. The vaginal microbiome contains at least 50 types of microorganisms that are actively involved in the formation of the microbial system of an infant long before birth, due to the formation of a special plantntal microbiome [30,31,32]. Almost any form of pathology of the female urogenital system is inextricably associated with a violation in the functioning of the microbiome [33].

The purpose of this study was to determine changes in the body's immunoreactivity for each macrotype of chronic endometritis, as well as determination of microbiological characteristics, alpha-2-microglobulin in blood serum

MATERIALS AND METHODS:

The study was conducted on the basis of the Rostov State Medical University. The study involved 610 women with a complicated obstetric history (failed IVF attempts, missed pregnancy, induced abortion, spontaneous abortion). The first group (retrospective analysis) - 200 women with a history of undeveloped pregnancy, an artificial abortion,
failures of in vitro fertilization (IVF) (pathomorphological verified CE); the second group (prospective analysis of 410 women) - similar cohorts of patients with early reproductive losses, with different frequency of morphological confirmation of CE. Microbiological research and diagnosis of deoxyribonucleic acid of possible pathogens of CE, determination of embiotropic autoantibodies in blood serum (ELI-P-test), determination of the content of alpha-2-microglobulin (AMGF) in menstrual blood, sonographic, hysteroscopic and pathomorphological studies (aspirates and biopsies from the cervical canal and uterus).

RESULTS AND DISCUSSION:

Poor patient management with early reproductive losses at the stage of emptying the uterine cavity, the absence of therapeutic measures predetermined the subsequent symptomatology of CE: the most typical was periodic pain in the lower abdomen in almost two-thirds of patients with spontaneous miscarriages and IVF failures in history (on average 71.3%) and the vast majority of women with missed pregnancies (81.5%) accompanying menorrhagia. The frequency of heavy and prolonged menstruation turned out to be the prerogative of all patients with non-developing pregnancies, while in the remaining cohorts it appeared in almost a comparable variant (on average 87.1%). Dysmenorrhea acted as a distinctive feature of patients with undeveloped pregnancy and spontaneous miscarriage practically a quarter (28.0%), while in other cohorts it appeared somewhat less frequently, on average 22.1%. Median menstrual flow was noted practically every sixth patient with an

artifactual abortion, undeveloped pregnancy and incompetent history of IVF attempts (on average 16.2%) and (10.3%) with spontaneous miscarriage. Abundant discharge of an inflammatory nature was noted mainly by patients with spontaneous miscarriage and undeveloped pregnancy (on average 61%), while in cohorts with artificial abortion and IVF failures, similar symptoms occurred in less than every second (46.8% in overall). Feeling of discomfort or pain during coitus was characteristic of a third of patients with early reproductive loss (33.1%), however, in the cohort with IVF failures, dyspareunia was recorded in only a quarter (23.6%). Dysuric disorders (frequent urination, pain, pain during urination) disturbed almost every seventh (16.1%) with an artifactual abortion, spontaneous miscarriage, unsuccessful IVF attempts, which is one and a half times less common than in the cohort with non-developing pregnancy (24.2%). Intoxication symptoms appeared in complaints of all patients, on average every tenth early reproductive losses (11.2%).

Hysteroscopic assessment of the state of the endometrium in early reproductive loss showed that endoscopic variants of CE (hyper-, hypoplastic and mixed) in cohorts are presented with equal frequency: 35.8, 31.9 and 32.3%.The specification of the nature of immunological and microbiological features was carried out for each of the CE macrotypes. Assessment of immunoreactivity in cohorts with miscarriage, tested on the basis of the ELIP test, showed a multidirectional response of each of the endoscopic CE variants: embryotropic autoantibodies were found to be excessive in half of the women (58.3%), which is twice as often as in other options (on average 22.6%).The greatest frequency of the pathological immune response has been determined in the hyperplastic variant (77.3%): with the dominant "poor" response (53.8%), the frequency of hyperreactivity coincided with episodes of production of a normal amount of embryotropic autoantibodies (average 23.5%). The frequency of hyporeactivity turned out to be the lowest at hypoplastic variant (11.3%), which is practically two times less often than with mixed, and more than 4 times - with hyperplastic macrotype (55.6%).

Glycodelin indicators were comparable low for all variants of early reproductive losses, however, the smallest indicator is determined at spontaneous miscarriage, (14.5 ± 3.9) ng / ml. The average levels of glycodelin in the menstrual blood of women with CE were significantly lower in comparison with the cohort without CE, (23.6 ± 3.2) ng / ml, with a hypoplastic macrotype, this indicator turned out to be two times less, (13.7 ± 3.6) ng / ml. Lactoflora deficiency appeared in the hypoplastic variant in two times more often than other macrotypes (13 and 7.8% on average), while normocenosis prevailed with mixed CE variant (12.4% versus 6.2% on average). The predominance of conditionally pathogenic flora with pronounced persistent characteristics and implementation in bacterial vaginosis was found in two thirds (71.2%) with a hypoplastic variant, more than half with mixed and hyperplastic macrotypes (on average 54.8%). Vaginitis episodes prevailed in the hyperplastic variant (33.1%), in the hypoplastic variant were recorded twice less often than in the hypoplastic type (12.0 and 24.4%, respectively). The cohort with a pH value of 4.5-5.0 was the vast majority of patients with hypoplastic macrotype (75.2%), two thirds of the remaining groups with CE (on average 60.3%). Vaginal pH value secretion of more than 5.0 was distinguished by every fifth patient with hyperplastic and mixed macrotypes (on average 23.9%), while in the hypoplastic variant CE - only every eighth (13.0%).

Comprehensive microbiological research with endoscopic macrotypes of CE (mixed, hypoplastic and hyperplastic) showed: detection of gram-positive microflora in the cervical channel (71.8; 72.1 and 66.7%, respectively), in a smaller the amount of gram-negative flora was determined (25.9%, 23.2% and 22.6%, respectively). Among the pathogenic microbes dominated by enterococcus - in 32.4% of women with a mixed macrotype of CE, in 43.8% with a hypoplastic macrotype, in 61% with a hyperplastic variant. A high content of Escherichia coli was found: to the greatest extent - with a hyperplastic variant (53.1%), one third (36.4%) - with mixed, each fifth (22.1%) - with hypoplastic CE macrotype. The seeding frequency of streptococcus was comparable for all endoscopic options (on average 15.9%), enterobacteriaceae - in every ninth with a mixed macrotype (11.2%), one and a half times more often - with other macrotypes (on average 17.5%). The prevalence of diplococci (on average 54.9%) with mixed and hyperplastic macrotypes with a dominant gonococcus (on average 15.3%. Bacterial-viral associations in patients with CE, which determine mixed infection, were detected mainly when hypoplastic variant in two thirds (77.0%), somewhat less often in hyperplastic variant (61.4%). With a mixed ChE macrotype, such mixed mixtures were recorded only in half (51.6%).

Infection screening by polymerase chain reaction (PCR) showed prevalence in cervical secretion in hypoplastic CE macrotype high titer (more than 104 CFU / ml) representatives conditionally pathogenic

flora in a third (39.5%) - M. hominis, in half (42.4% each) - U. Urealyticum and G. vaginalis, in a quarter of patients (28.3%) - C. albicans. The lowest frequency of contamination by the indicated infects was noted in the mixed variant of CE, in a quarter of which (on average, 26.1%) prevailed U. urealyticum and G. vaginalis. The high frequency of Ch.tracomatis is a distinctive feature of the microbiota of every second patient with hyperplastic macrotype CE (41.4%), in other cases it is almost three times less frequent (on average 16.5%). The frequency of carriage of cytomegalovirus (CMV) was comparable (13.0; 17.2 and 16.9%) against the background of the prevalence of herpes simplex virus (HSV) in hypo- and hyperplastic variants of CE (on average 56.8%).The frequency of sterile cultures was found to be practically comparable with the mixed variant of CE every sixth patient with different types of immunoreactivity (on average, 17%). The smallest number of cases of normoreactivity accompanying the absence of flora growth was recorded in the hyperplastic type of CE (9%).

The category "opportunistic flora" was in the lead in the cohort of hyperreactive patients (97.1%) with hypoplastic CE macrotype; it was somewhat less common with hyporeactivity in the rest of the examined women (on average 88%). It is noteworthy that carriage of such infections was observed in half of women with a normal amount of embryotropic autoantibodies (50.2%) with mixed and hypoplastic macrotypes, which is three times more often than with hyperplastic CE. Detection of a specific pathogen was determined mainly in a cohort of hyporeactive patients with a hyperplastic type of ChE (90.7%), almost one and a half times less often - in hyperreactive (77.4%). With mixed option, the frequency of detection of pathogenic infections turned out to be comparable, regardless of the type of immunoreactivity (on average, 43.2%), with hypoplastic - it was recorded in a third with abnormal production of embryotropic autoantibodies (on average, 34.2%) and in a quarter with normoreactivity (24.3%).

Bacterial-viral associations were recorded in the vast majority of hyperreactive patients (93.9%) with hypoplastic macrotype and more than half - with mixed (60.9%). Hyporeactivity of the immune system in the presence of such mixes was found mainly in the hyperplastic macrotype (86.2%), less often than others - with the mixed variant of CE (68.6%).The frequency of normal production of embryotropic autoantibodies with the carriage of a number of associates was the lowest in cohort with hyperplastic macrotype (13%), then with other variants, CE was comparable to three times higher (on average 37.9%).The bacterial mycotic mixture was the prerogative of hyporeactive representatives with a hyperplastic ChE macrotype (almost two thirds), while in other cases, a “poor” immune response was recorded only in half. Hyperreactivity to the presence of such a microbial association turned out to be the highest in cohort with hyperplastic macrotype (48.3%), in of other women with CE, a variant of a similar immune response was recorded in every fifth (in average 18.7%).The frequency of normal production of embryotropic autoantibodies was minimal in hypoplastic CE (6%), however, in representatives with a mixed macrotype practically “competed” with hyporeactivity (45 and 52.1%, respectively). Note the dominant in hypoplastic ChE macrotype of hyperreactivity, which determines the development of autoimmune processes, in hyperplastic - hyporeactive changes accompanied by an increase in the frequency of infection by associations of opportunistic bacteria, which correlates with data from other researchers.

CONCLUSION:

In the pathogenesis of reproductive disorders in women with CE, various immuno-microbiological aspects appear. Vaginal persistence of conditionally pathogenic flora in “aggressive” titles is a sad “decoration” to the prologue about CE, the tragic outcome is predetermined by the surgical stress-mechanical trauma of the uterine tissues, coupled with the lack of control of endoscopic imaging. To preserve the pregnancy, it is necessary to remember about the multifactorial nature of CE genesis and to use multidimensional restorative therapy of structural and functional disorders of the endometrium with variable immunocorrection and the achievement of eubiosis of genitals.

List of symbols and Abbreviations:
CE - chronic endometritis,
IVF - in vitro fertilization.

REFERENCES:

1. Jin LP, Fan DX, Zhang T, Guo PF, Li DJ. The costimulatory signal upregulation is associated with Th1 bias at the maternal-fetal interface in human miscarriage. Am J Reprod Immunol. 2011;66:270–278.
2. Petrov YuA, Kovaleva EA. The valid duration of use plastic intrauterine contraceptives. Obstetrics and Gynecology, 1986; 7: 40.
3. Sfakianoudis K, Simopoulou M, Nikas Y, Rapani A, Nitsos N., et al. Efficient treatment of chronic endometritis through a novel approach of

intrauterine antibiotic infusion: a case series. BMC Womens Health, 2018; 18: 197.
4. Arabestani MR, Fazzeli H, Nasr Esfahani B. Identification of the most common pathogenic bacteria in patients with suspected sepsis by multiplex PCR. J Infect Dev Ctries, 2014;8:461-8.
5. Petrov YuA. Oncological risk assessment of intrauterine contraception based on cytological studies of the endometrium. Problems in oncology, 1985;12:53-56.
6. 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
7. 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.
8. Petrov YuA, Kovaleva EA. Features of colpocytograms of women using intrauterine contraception. Klinicheskaya Laboratornaya Diagnostika, 1986;1: 51-52.
9. 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.
10. Baker JM, Chase DM, Herbst-Kralovetz MM. Uterine microbiota: Residents, tourists, or invaders? Front Immunol, 2018; 9: 208.
11. 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.
12. Tortorella C, Piazzolla G, Matteo M, Pinto V, Tinelli R, Sabba C, et al. Interleukin-6, interleukin-1β, and tumor necrosis factor α in menstrual effluents as biomarkers of chronic endometritis. Fertil Steril. 2014;101:242–247.
13. Petrov YuA. Features of hyperplastic processes of the uterine mucosa in women using intrauterine contraceptives. Problems of maternity and child care, 1985; 11:67.
14. Chen C, Song X, Wei W, et al. The microbiota continuum along the female reproductive tract and its relation to uterine-related diseases. Nat Commun, 2017; 8: 875.
15. Petrov YuA, Rymashevsky NV, Kovaleva EA. Endometrial condition with intrauterine contraception. Problems of maternity and child care, 1988;3:59-62.
16. Cicinelli E, Matteo M, Tinelli R, et al. Prevalence of chronic endometritis in repeated unexplained implantation failure and the IVF success rate after antibiotic therapy. Hum Reprod, 2015; 30: 323– 330.
17. Kupina AD, Petrov YuA. Efficiency of sonographic research in diagnostics of chronic endometritis. Indo American Journal of Pharmaceutical Sciences, 2019; 6(11):15210-15213.
18. Di Pietro C, Cicinelli E, Guglielmino MR, et al. Altered transcriptional regulation of cytokines, growth factors, and apoptotic proteins in the endometrium of infertile women with chronic endometritis. Am J Reprod Immunol, 2013; 69: 509– 517.
19. Di Spiezio Sardo A, Di Carlo C, Minozzi S, et al. Efficacy of hysteroscopy in improving reproductive outcomes of infertile couples: a systematic review and meta-analysis. Hum Reprod Update, 2016;22:479–496.
20. Humbert C, Silbermann F, Morar B, et al. Integrin alpha 8 recessive mutations are responsible for bilateral renal agenesis in humans. American Journal of Human Genetics, 2014; 94(2):288.
21. Kamińska D, Gajecka M. Is the role of human female reproductive tract microbiota underestimated? Benef Microbes, 2017; 8:327–433.
22. Kitaya K, Matsubayashi H, Yamaguchi K, et al. Chronic endometritis: potential cause of infertility and obstetric and neonatal complications. Am J Reprod Immunol, 2016;75:13–22.
23. Kimura F, Takebayashi A, Ishida M, et al. Review: Chronic endometritis and its effect on reproduction. Journal of Obstetrics and Gynaecology Researc, 2015; 30(2):323-330.
24. Kitaya K, Takeuchi T, Mizuta S, et al. Endometritis: new time, new concepts. Fertility and Sterility, 2018;110(3):344–350.
25. Di Pietro C, Cicinelli E, Guglielmino MR, Ragusa M, Farina M, Palumbo MA, et al. Altered transcriptional regulation of cytokines, growth factors, and apoptotic proteins in the endometrium of infertile women with chronic endometritis. Am J Reprod Immunol. 2013;69:509–517.
26. Gibreel A, El-Adawi N, Elgindy E, Al-Inany H, Allakany N, Tournaye H. Endometrial scratching for women with previous IVF failure undergoing IVF treatment. Gynecol Endocrinol. 2015;31:313–316.
27. Liu Y, Chen X, Huang J, et al. Comparison of the prevalence of chronic endometritis as determined by means of different diagnostic methods in women with and without

reproductive failure. Fertil Steril, 2018; 109: 832– 839.
28. Moreno I, Cicinelli E, Garcia-Grau I, et al. The diagnosis of chronic endometritis in infertile asymptomatic women: a comparative study of histology, microbial cultures, hysteroscopy, and molecular microbiology. American Journal of Obstetrics & Gynecology, 2018; 218(6): 602.e1-602.e16.
29. Vitagliano A, Saccardi C, Noventa M, et al. Effects of chronic endometritis therapy on in vitro fertilization outcome in women with repeated implantation failure: A systematic review and meta-analysis. Fertil Steril, 2018; 110: 103– 112.
30. Adegboyega PA, Pei Y, McLarty J. Relationship between eosinophils and chronic endometritis. Hum Pathol. 2010;41:33–37.
31. 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.
32. Bouet PE, El Hachem H, Monceau E, Gariepy G, Kadoch IJ, Sylvestre C. Chronic endometritis in women with recurrent pregnancy loss and recurrent implantation failure: prevalence and role of office hysteroscopy and immunohistochemistry in diagnosis. Fertil Steril, 2016;105:106–110.
33. Petrov YuA, Dolzhenkova LM. Histochemical examination of glycogen in the endometrium of women using intrauterine contraceptives. Obstetrics & Gynecology. 1985; 9: 57.