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**CORRECTION OF REPRODUCTIVE SYSTEM DISORDERS BY
MODERN METHODS IN WOMEN WITH ENDOMETRITIS AFTER
MISCARRIAGE**

Resume: In recent years, inflammatory diseases of the reproductive system remain a problem with its relevance, continuing to occupy one of the first places among the causes of diseases of the reproductive system.

This article explains that in women with reproductive diseases and in modern conditions, the high frequency of chronic endometritis does not tend to decrease, the problem of inflammatory diseases of the female reproductive system remains an urgent medical and social problem today, inflammatory diseases of the reproductive system continue to occupy one of the first places among the causes of reproductive, along with chronic inflammatory diseases of the vagina and uterine appendages, there has recently been an increase in the frequency of chronic endometritis (CE) and other data are presented.

This article provides information that, according to the materials of various researchers, its frequency is on average from 14 to 25%.

Keywords: reproductive system, miscarriage, endometritis, inflammation of the female genital organ.

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**КОРРЕКЦИЯ НАРУШЕНИЙ РЕПРОДУКТИВНОЙ СИСТЕМЫ
СОВРЕМЕННЫМИ МЕТОДАМИ У ЖЕНЩИН С ЭНДОМЕТРИТОМ
ПОСЛЕ НЕВЫНАШИВАНИЯ БЕРЕМЕННОСТИ**

Резюме: В последние годы воспалительные заболевания репродуктивной системы остаются проблемой с ее актуальностью, продолжая занимать одно из первых мест среди причин заболеваний репродуктивной системы.

В данной статье объясняется, что у женщин с репродуктивными заболеваниями и в современных условиях высокая частота хронического эндометрита не имеет тенденции к снижению, проблема воспалительных заболеваний женской репродуктивной системы остается актуальной медицинской и социальной проблемой на сегодняшний день, воспалительные заболевания репродуктивной системы продолжают занимать одно из первых мест среди причин репродуктивного, наряду с хроническими воспалительными заболеваниями влагалища и придатков матки в последнее время наблюдается увеличение частоты хронического эндометрита (ХЭ) и представлены другие данные.

В этой статье приводится информация о том, что, согласно материалам различных исследователей, его частота составляет в среднем от 14 до 25%.

Ключевые слова: репродуктивная система, невынашивания беременности, эндометрит, воспаления женского полового органа.

Relevance. Chronic endometritis (CE), despite numerous scientific studies and information about its significant prevalence (60-65%), continues to be the terra incognita of modern gynecology[5,8,9].

The significance of this nosology is determined by the significant difficulties of its recognition, however, we believe insufficient attention of specialists to the need to optimize the prevention and treatment of women with CE as a reserve for increasing fertility. The consistently high frequency of HE refutes the involvement of the problem in the category of banal, moreover, the contraversions of recent years postulate a departure from the one-sided

perception of the disease exclusively as a classic purulent-inflammatory process, complicating, according to statistics, every 4-5 surgical abortion [2,4,7]. It is sad to state, however, there is no "dissection" of HE in the context of the root cause of early reproductive losses from the standpoint of annual demographic and economic losses of society. Such omissions form an "artifact" policy of therapeutic and diagnostic measures, moreover, a whole cohort of women with undiagnosed HE is out of the field of view of gynecologists, which, in the absence of full-fledged rehabilitation therapy and pre-pregnancy training, closes the vicious circle of habitual miscarriage in more than 70% [1,6,7].

The conceptual moment that destroys the stereotypical ideas about HE as an exclusively gynecological problem was the conclusion of the FIGO session (Kuala Lumpur, 2006), postulating that chronic inflammation of the uterus is the cause of NB.

Unsuccessful emptying of the uterus outside of hysteroscopic imaging and full rehabilitation of the injured endometrium forms the essence of iatrogenic CE, as well as infection of the endometrium when using an intrauterine contraceptive (IUD).

The absence of a unified concept of the pathogenesis of HE, revealing the mechanisms of formation and interrelation of various pathological processes in the endometrium, understanding the basis of the violation of its macro- and microscopic functions, a comprehensive analysis that takes into account the features of the structure and function of the uterine mucosa, prevents the implementation of reasonable therapy, aggravating the existing reproductive ill health of women of fertile age.

Microbiological diagnostics is recognized as a "weak link" in the detection of HE: the frequent absence of a microbial agent in endometrial samples or, on the contrary, the persistence of conditionally pathogenic flora affects the rhetorical question of an infectious trigger to this day [2,4,9].

There are noteworthy indications of a possible relationship between HE and the proliferative processes of the endometrium, however, the question of the correlation of the mechanisms of regulation of programmed cell death of endometrial cells with different receptor status and morphostructural features remains open. In this regard, a comprehensive comparative analysis of the balance of apoptosis and proliferation processes in CE is relevant, along with an assessment of the involvement of various microbial agents in endometrial regulation [3,5,8]. Despite separate studies of impaired expression of stromal and epithelial steroid receptors, immunohistochemical markers of endometrial receptivity, the pro-inflammatory orientation of immunological reactions in CE is presented fragmentally [2,8].

The ambiguity of the correlation of clinical, echographic and histological characteristics completes the probability of diagnostic errors, therefore, the attention of specialists should be focused on the histopathic features of each of the HE variants [1,4,9]. The variability of the results of the pathomorphological assessment of the endometrium also makes one doubt the absolute informativeness of the method, obviously, due to the differences in the methods used [6,8]. There are few data on the cytological features of the composition of metroaspirates in cohorts with early pregnancy losses, due attention is not paid to cytomorphology as a significant method for predicting the complicated course of the post-abortion period with its proven informativeness in puerperia.

There are isolated studies of the variability of adaptive reactions with a change in the nonspecific resistance of the organism not only at the stage of the initial response to damaging effects, but also the speed, adequacy of the restructuring of protective forces in response to the restoration of immunoreactivity after illness or effectively carried out therapeutic measures.

The unfavorable prognosis of the course of HE is largely due to the lack of an algorithmized approach in the diagnosis and treatment of this nosology, while awareness of the immunological events accompanying various variants of HE

will allow differentiated prescribing of immunocorrective therapy. The analysis of scientific papers disappoints the lack of emphasis on the need to preserve and restore the reproductive health of the contingent after the loss of pregnancy, since the frequency of such determines the growth and HE.

The development of a comprehensive system for the diagnosis and treatment of this nosology, the emphasis on the importance of the pre-gravidar stage are an important vector for solving the problem of preserving reproductive potential in women with HE.

The aim of the study: to improve the methods of prevention, diagnosis and treatment of chronic endometritis (CE) in women of reproductive age.

Materials and methods of research. To achieve this goal, a prospective analysis of hysteroscopic characteristics in a cohort with morphologically proven CE in 94 patients with a history of early reproductive losses was carried out.

The results of the study. An analysis of episodes of the contraceptive "history" of residents of the Andijan region showed a steady decline in the popularity of the IUD, and, according to the labels "is registered at the dispensary" and "taken again", the trend is the same. During the specified interval, the number of women being observed as dispensary users of the IUD decreased by 1, due to the change in contraceptive policy.

Despite the unequivocal tendency to decrease early reproductive losses due to artificial abortions, the statistics of post-abortion complications did not differ in a uniform decrease.

The questionable informativeness of hysteroscopic imaging in the diagnosis of HE due to a number of methodological defects can distort the real picture, negatively affecting the pathomorphological conclusion, as a result of which we consider it justified to reduce macroscopic signs of the inflammatory process in the uterine mucosa to the visually dominant endoscopic type. A descriptive picture of hysteroscopic variants of HE was present in the works

earlier (Podzolkova N.M. et al., 2004), however, the effectiveness of techniques in its recognition has not been evaluated, there is no analysis of a detailed correlation of the basic changes in the hysteroscopic structure of the endometrium with the functional dissonance of all components of the mucosa itself.

To achieve this goal, a prospective analysis of hysteroscopic characteristics in a cohort with morphologically proven CE in 94 patients with a history of early reproductive losses was carried out. When analyzing hysteroscopic "findings", the whole variety of variants was reduced to three macrotypes, allowing further, taking into account morphological verification, to avoid diagnostic errors.

The selection of hysteroscopic macrotypes – hyperplastic, hypoplastic, mixed - was carried out on the basis of grouping of signs characterizing the thickness, color and structure of the mucosa, the severity of the vascular pattern in the presence of a chronic inflammatory process.

The extrapolation of the macrotypes to the prospectively studied group with early reproductive losses made it possible to verify the non-specificity of the results of echographic and hysteroscopic studies in relation to the layout according to the variants of early reproductive losses and their true informativeness within the framework of the selection of macrotypes.

Questionable samples with incomplete morphological picture of HE were recorded in 15.3% with mixed macrotype, 14.9% - hyperplastic, 25.9% - hypoplastic.

The isolation of morphological signs of HE with distribution by macrotypes showed variability in the structure of the mucosa with pronounced inflammatory infiltration of its stroma by lymphocytes: focal - mainly with hypoplastic macrotype (69.2%) ($p < 0.05$) and diffuse - with hyperplastic (80.7%) ($p < 0.05$) and mixed (68.5%) ($p < 0.05$).

It is necessary to refute the fact that plasma cells must be detected in CE: in cohorts - in two-thirds with mixed and hyperplastic macrotype (79.3% and 71.1%, respectively) and half - hypoplastic (53.3%) ($p < 0.05$).

Dystrophic-atrophic damage to the cells of the basal and glandular layers of the endometrium, reflecting the intensification of apoptosis of the integumentary epithelial cells and glandulocytes of the mucosa with low proliferative activity, were the prerogative of representatives with a hypoplastic variant of HE (85%). When mixed, such changes were almost twice as rare (37.8%) ($p < 0.05$).

The final interpretation of the occurrence of CE in cohorts with early reproductive losses indicates the presence of it in 90% of women with SV, 91.7% - with NB, 83.3% - with failed IVF attempts, 85.7% of women with complaints and a history of AA. High frequency of CE detection on the background of placental tissue residues (after AA – 25.8%, CB – 28.3%!) it refers to the need for instrumental emptying of the uterus under the control of imaging (ultrasound, hysteroscopy) and the development of standardized rehabilitation techniques depending on the variant of the macrotype.

The indicator of focal stroma fibrosis prevailed in the contingent with unsuccessful IVF attempts (7.6%), which is five times more than in the representatives with CB (1.7%) ($p < 0.05$), almost one and a half – NB (4.8%), three – AA (2.5%). There are isolated indicators of the occurrence of endometrial polyp (focal hyperplasia), however, in the cohort with unsuccessful IVF attempts, this nosology was twice as rare as the conclusion about the absence of endometrial pathology (3% vs. 6.1%).

Taking into account the final verification of HE for each macrotype, the effectiveness of the method for recognizing the chronic inflammatory process in the uterine mucosa was evaluated.

The echographic method of investigation does not have sufficient resolution in detecting CE and cannot be reliable for accurate diagnosis of the

disease due to the fact that the diagnostic value for detecting macrotypes ranges from 81.2% to 83.1%.

The hysteroscopic method is more informative, the potential of which varies already within higher limits (DT – from 87.5% to 94.2%).

The morphological method of investigation should be considered highly informative, highly specific and diagnostically accurate, but we have demonstrated the possibility of obtaining more detailed information when using immunohistochemical methods in the diagnosis of HE.

The results of the assessment of the cytological picture of metroaspirates of women with various variants of reproductive losses in early pregnancy immediately after instrumental intervention allow us to conclude about the high prognostic significance of the method.

Combined morphological changes underlying early pregnancy losses were identified: chronic productive inflammation (parietal and basal deciduitis) with zones of microabscesses in the uteroplacental region and local hemostasis disorders in the parietal endometrium and d.basalis (delaminating hemorrhages, thrombosis, retroplacental hematoma). This fact only confirms the relevance of the conclusions about a local systemic inflammatory response with a multi-link reaction, even at the tissue level. A similar pattern was found in all women with NB, SV, IVF failures (100%) and in 25.7% - with AA.

Correlation of the results of cytological evaluation of metroaspirates with morphological data showed the presence of inflammatory process of the uterine mucosa in 52 women without hysteroscopic control during emptying of the uterine cavity.

The evaluation of immunoreactivity in cohorts with pregnancy losses tested on the basis of the ELIP test showed a multidirectional reaction of each of the endoscopic variants of HE not only in intra-group comparison, but also with healthy women. Abnormal production of embryotropic autoantibodies was

detected in 78.1% of women with hyperplastic macrotype CE, 75.7% - with mixed, 80% - with hypoplastic, but its nature is multidirectional.

A comprehensive microbiological study at all levels allowed us to state the involvement of dysbiotic disorders in infection of the cervical canal and uterine mucosa (confirmation – bacterioscopy, pH-metry) – in the vast majority of all patients with CE, to the greatest extent – with hypoplastic macrotype (87.5%) ($p < 0.05$).

Assessment of concordance of infection of the cervical canal and endometrium it convinces of the diverse predominance of microbial representatives with unequal occurrence in different niches.

Conclusions. The frequency of chronic endometritis in cohorts with a history of early reproductive losses is: with spontaneous miscarriage – in 90%, 91.7% - with an undeveloped pregnancy, 83.3% - with failed IVF attempts, 85.7% of women with an artificial abortion. The diagnosis of chronic endometritis against the background of placental tissue remains after an artificial abortion reaches 25.8%, spontaneous abortion – 28.3%. The failure of the immune response in hypoplastic macrotype is realized in the dominant of stress reactions (chronic stress reaction), hyperactivity, inhibition of cell-mediated reactions (decrease in CD4+, immunoregulatory index CD4+ /CD8+, natural killers C16+, IgG, IgM, pronounced – phagocytosis link against the background of CD95+ induction and increased values of IdA and the CEC).

A high probability of maintaining stress adaptive reactions, the predominance of abnormal production of embryotropic autoantibodies and immune imbalance in traditional therapy of chronic endometritis was documented in 25.1% of women.

The effectiveness of the proposed methods of rehabilitation of women with chronic endometritis is determined by the high probability of the realization of reproductive function in 69.5%.

A comprehensive system for the prevention of the development of chronic endometritis after early reproductive losses, based on the priority of medical abortion, if it is impossible – visual control (ultrasound / hysteroscopy) emptying of the uterine cavity, perabort rehabilitation, immediate post-abortion rehabilitation, cytological examination of metroaspirates allows women to recover twice as much as the traditional course, four or five times more than its absence.

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